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(71) Applicant: **SCHERING CORPORATION** [US/US];  
2000 Galloping Hill Road, Kenilworth, NJ 07033-0530  
(US).

(72) Inventor: **GORMAN, Daniel, M.**; 6371 Central Avenue,  
Newark, CA 94560 (US).

(74) Agent: **ZARADIC, Sandy**; Schering-Plough Corpora-  
tion, Patent Department, K-6-1, 1990, 2000 Galloping Hill  
Road, Kenilworth, NJ 07033-0530 (US).

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**WO 01/90358 A2**

(54) Title: MAMMALIAN RECEPTOR PROTEINS; RELATED REAGENTS AND METHODS

(57) Abstract: Nucleic acids encoding mammalian, e.g., primate, receptors, purified receptor proteins and fragments thereof. Anti-  
bodies, both polyclonal and monoclonal, are also provided. Methods of using the compositions for both diagnostic and therapeutic  
utilities are described.

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## MAMMALIAN RECEPTOR PROTEINS; RELATED REAGENTS AND METHODS

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## FIELD OF THE INVENTION

The present invention relates to compositions and methods for affecting mammalian physiology, including immune system function. In particular, it provides methods to regulate development and/or the immune system. Diagnostic and therapeutic uses of these materials are also disclosed.

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## BACKGROUND OF THE INVENTION

Recombinant DNA technology refers generally to techniques of integrating genetic information from a donor source into vectors for subsequent processing, such as through introduction into a host, whereby the transferred genetic information is copied and/or expressed in the new environment. Commonly, the genetic information exists in the form of complementary DNA (cDNA) derived from messenger RNA (mRNA) coding for a desired protein product. The carrier is frequently a plasmid having the capacity to incorporate cDNA for later replication in a host and, in some cases, actually to control expression of the cDNA and thereby direct synthesis of the encoded product in the host. See, e.g., Sambrook, et al. (1989) Molecular Cloning: A Laboratory Manual, (2d ed.) vols. 1-3, CSH Press, NY.

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For some time, it has been known that the mammalian immune response is based on a series of complex cellular interactions, called the "immune network". Recent research has provided new insights into the inner workings of this network. While it remains clear that much of the immune response does, in fact, revolve around the network-like interactions of lymphocytes, macrophages, granulocytes, and other cells, immunologists now generally hold the opinion that soluble proteins, known as lymphokines, cytokines, or monokines, play critical roles in controlling these cellular interactions. Thus, there is considerable interest in the isolation, characterization, and mechanisms of action of cell modulatory factors, an understanding of which will lead to significant advancements in the diagnosis and therapy of numerous medical abnormalities, e.g., immune system disorders.

The immune system of vertebrates consists of a number of organs and several different cell types. Two major cell types include the myeloid and lymphoid lineages. Among the lymphoid cell lineage are B cells, which were originally characterized as differentiating in fetal liver or adult bone marrow, and T cells, which were originally characterized as differentiating in the thymus. See, e.g., Paul (ed. 1998) Fundamental Immunology (4th ed.) Raven Press, New York; and Thomson (ed. 1994) The Cytokine Handbook 2d ed., Academic Press, San Diego. Lymphokines apparently mediate cellular activities in a variety of ways. They have been shown to support the proliferation, growth, and/or differentiation of cells, e.g., pluripotential hematopoietic stem cells, into vast numbers of progenitors comprising diverse cellular lineages which make up a complex immune system. Proper and balanced interactions between the cellular components are necessary for a healthy immune response. The different cellular lineages often respond in a different manner when lymphokines are administered in conjunction with other agents.

Cell lineages especially important to the immune response include two classes of lymphocytes: B-cells, which can produce and secrete immunoglobulins (proteins with the capability of recognizing and binding to foreign matter to effect its removal), and T-cells of various subsets that secrete lymphokines and induce or suppress the B-cells and various other cells (including other T-cells) making up the immune network. These lymphocytes interact with many other cell types.

Research to better understand and treat various immune disorders has been hampered by the general inability to maintain cells of the immune system in vitro. Immunologists have discovered that culturing many of these cells can be accomplished through the use of T-cell and other cell supernatants, which contain various growth factors, including many of the lymphokines.

Various growth and regulatory factors exist which modulate morphogenetic development. And many receptors for cytokines are also known. Often there are at least two critical subunits in the functional receptor. See, e.g., Gonda and D'Andrea (1997) Blood 89:355-369; Presky, et al. (1996) Proc. Nat'l Acad. Sci. USA 93:14002-14007; Drachman and Kaushansky (1995) Curr. Opin. Hematol. 2:22-28; Theze (1994) Eur. Cytokine Netw. 5:353-368; and Lemmon and Schlessinger (1994) Trends Biochem. Sci. 19:459-463.

From the foregoing, it is evident that the discovery and development of new soluble proteins and their receptors, including ones similar to lymphokines, should contribute to new therapies for a wide range of degenerative or abnormal conditions which directly or indirectly involve development, differentiation, or function, e.g., of the

immune system and/or hematopoietic cells. In particular, the discovery and understanding of novel receptors for lymphokine-like molecules which enhance or potentiate the beneficial activities of other lymphokines would be highly advantageous. However, the lack of understanding of how the immune system is regulated or differentiates has blocked the ability to advantageously modulate the normal defensive mechanisms to biological challenges. Medical conditions characterized by abnormal or inappropriate regulation of the development or physiology of relevant cells thus remain unmanageable. The discovery and characterization of specific cytokines and their receptors will contribute to the development of therapies for a broad range of degenerative or other conditions which affect the immune system, hematopoietic cells, as well as other cell types. The present invention provides new receptors for ligands exhibiting similarity to cytokine like compositions and related compounds, and methods for their use.

#### SUMMARY OF THE INVENTION

The present invention is directed to novel receptors related to cytokine receptors, e.g., primate, cytokine receptor like molecular structures, designated DNAX Cytokine Receptor Subunits (DCRS), and their biological activities. In particular, it provides description of various subunits, designated DCRS6, DCRS7, DCRS8, DCRS9, and DCRS10. Primate, e.g., human, and rodent, e.g., mouse, embodiments of the various subunits are provided. It includes nucleic acids coding for the polypeptides themselves and methods for their production and use. The nucleic acids of the invention are characterized, in part, by their homology to cloned complementary DNA (cDNA) sequences enclosed herein.

The present invention provides a composition of matter selected from: a substantially pure or recombinant polypeptide comprising at least three distinct nonoverlapping segments of at least four amino acids identical to segments of SEQ ID NO: 2, 5, 8, 11, 23, or 26; a substantially pure or recombinant polypeptide comprising at least three distinct nonoverlapping segments of at least four amino acids identical to segments of SEQ ID NO: 14; a substantially pure or recombinant polypeptide comprising at least two distinct nonoverlapping segments of at least five amino acids identical to segments of SEQ ID NO: 14; a natural sequence DCRS8 comprising mature SEQ ID NO: 14; a fusion polypeptide comprising DCRS8 sequence; a substantially pure or recombinant polypeptide comprising at least three distinct nonoverlapping segments of at least four amino acids identical to segments of SEQ ID NO: 17 or 20; a substantially pure or recombinant polypeptide comprising at least two distinct nonoverlapping segments of at least five amino acids identical to segments of SEQ ID NO: 17 or 20; a natural



sequence DCRS9 comprising mature SEQ ID NO: 17 or 20; or a fusion polypeptide comprising DCRS9 sequence. Preferably, wherein the distinct nonoverlapping segments of identity include: one of at least eight amino acids; one of at least four amino acids and a second of at least five amino acids; at least three segments of at least four, five, and six amino acids, or one of at least twelve amino acids. In other embodiments, the:  
5 polypeptide: comprises a mature sequence of Tables 1, 2, 3, 4, or 5; is an unglycosylated form of DCRS8 or DCRS9; is from a primate, such as a human; comprises at least seventeen amino acids of SEQ ID NO: 14 or 17; exhibits at least four nonoverlapping segments of at least seven amino acids of SEQ ID NO: 14 or 17; is a natural allelic  
10 variant of DCRS8 or DCRS9; has a length at least about 30 amino acids; exhibits at least two non-overlapping epitopes which are specific for a primate DCRS8 or DCRS9; is glycosylated; has a molecular weight of at least 30 kD with natural glycosylation; is a synthetic polypeptide; is attached to a solid substrate; is conjugated to another chemical moiety; is a 5-fold or less substitution from natural sequence; or is a deletion or insertion  
15 variant from a natural sequence.

The invention further embraces a composition comprising: a substantially pure DCRS8 or DCRS9 and another cytokine receptor family member; a sterile DCRS8 or DCRS9 polypeptide; the DCRS8 or DCRS9 polypeptide and a carrier, wherein the carrier is: an aqueous compound, including water, saline, and/or buffer; and/or formulated for  
20 oral, rectal, nasal, topical, or parenteral administration. Additional embodiments include a polypeptide comprising: mature protein sequence of Tables 1, 2, 3, 4, or 5; a detection or purification tag, including a FLAG, His6, or Ig sequence; or sequence of another cytokine receptor protein. Kit embodiments include ones comprising a described polypeptide, and: a compartment comprising the protein or polypeptide; or instructions  
25 for use or disposal of reagents in the kit.

Binding compositions are provided, e.g., comprising an antigen binding site from an antibody, which specifically binds to a natural DCRS8 or DCRS9 polypeptide, wherein: the binding compound is in a container; the DCRS8 or DCRS9 polypeptide is from a human; the binding compound is an Fv, Fab, or Fab2 fragment; the binding  
30 compound is conjugated to another chemical moiety; or the antibody: is raised against a peptide sequence of a mature polypeptide of Table 3 or 4; is raised against a mature DCRS8 or DCRS9; is raised to a purified human DCRS8 or DCRS9; is immunoselected; is a polyclonal antibody; binds to a denatured DCRS8 or DCRS9; exhibits a Kd to antigen of at least 30  $\mu$ M; is attached to a solid substrate, including a bead or plastic membrane; is  
35 in a sterile composition; or is detectably labeled, including a radioactive or fluorescent label. Kits include ones comprising such a binding compound, and: a compartment

comprising the binding compound; or instructions for use or disposal of reagents in the kit.

The invention also provides methods of producing an antigen:antibody complex, comprising contacting under appropriate conditions a primate DCRS8 or DCRS9 polypeptide with a described antibody, thereby allowing the complex to form. Preferred methods include ones wherein: the complex is purified from other cytokine receptors; the complex is purified from other antibody; the contacting is with a sample comprising an interferon; the contacting allows quantitative detection of the antigen; the contacting is with a sample comprising the antibody; or the contacting allows quantitative detection of the antibody. Further compositions include those comprising: a sterile binding compound, as described, or the binding compound and a carrier, wherein the carrier is: an aqueous compound, including water, saline, and/or buffer; and/or formulated for oral, rectal, nasal, topical, or parenteral administration.

Nucleic acid compositions include an isolated or recombinant nucleic acid encoding a described polypeptide wherein the: DCRS8 or DCRS9 is from a human; or the nucleic acid: encodes an antigenic peptide sequence of Table 3 or 4; encodes a plurality of antigenic peptide sequences of Table 3 or 4; exhibits identity over at least thirteen nucleotides to a natural cDNA encoding the segment; is an expression vector; further comprises an origin of replication; is from a natural source; comprises a detectable label; comprises synthetic nucleotide sequence; is less than 6 kb, preferably less than 3 kb; is from a primate; comprises a natural full length coding sequence; is a hybridization probe for a gene encoding the DCRS8 or DCRS9; or is a PCR primer, PCR product, or mutagenesis primer. Also provided are a cell or tissue comprising such a recombinant nucleic acid, e.g., where the cell is: a prokaryotic cell; a eukaryotic cell; a bacterial cell; a yeast cell; an insect cell; a mammalian cell; a mouse cell; a primate cell; or a human cell.

Kit embodiments include those comprising a described nucleic acid and: a compartment comprising the nucleic acid; a compartment further comprising a primate DCRS8 or DCRS9 polypeptide; or instructions for use or disposal of reagents in the kit.

Other nucleic acids provided include ones which: hybridize under wash conditions of 30 minutes at 30° C and less than 2M salt to the coding portion of SEQ ID NO: 13 or 16; or exhibit identity over a stretch of at least about 30 nucleotides to a primate DCRS8 or DCRS9. Preferably, such will be nucleic acids where: the wash conditions are: at 45° C and/or 500 mM salt; at 55° C and/or 150 mM salt; or the stretch is at least 55 or 75 nucleotides.

Also provided are methods of modulating physiology or development of a cell or tissue culture cells comprising contacting the cell with an agonist or antagonist of a

mammalian DCRS8 or DCRS9. Preferably, the cell is transformed with a nucleic acid encoding the DCRS8 or DCRS9 and another cytokine receptor subunit.

## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

5

### OUTLINE

- I. General
- II. Activities
- III. Nucleic acids
  - 10 A. encoding fragments, sequence, probes
  - B. mutations, chimeras, fusions
  - C. making nucleic acids
  - D. vectors, cells comprising
- IV. Proteins, Peptides
  - 15 A. fragments, sequence, immunogens, antigens
  - B. muteins
  - C. agonists/antagonists, functional equivalents
  - D. making proteins
- V. Making nucleic acids, proteins
  - 20 A. synthetic
  - B. recombinant
  - C. natural sources
- VI. Antibodies
  - 25 A. polyclonals
  - B. monoclonal
  - C. fragments; Kd
  - D. anti-idiotypic antibodies
  - E. hybridoma cell lines
- VII. Kits and Methods to quantify DCRSs
  - 30 A. ELISA
  - B. assay mRNA encoding
  - C. qualitative/quantitative
  - D. kits
- VIII. Therapeutic compositions, methods
  - 35 A. combination compositions
  - B. unit dose
  - C. administration
- IX. Screening
- X. Ligands

40

### I. General

The present invention provides the amino acid sequence and DNA sequence of mammalian, herein primate, cytokine receptor-like subunit molecules, these designated DNAX Cytokine Receptor Subunits 6 (DCRS6), 7 (DCRS7), 8 (DCRS8), 9 (DCRS9),  
45 and 10 (DCRS10) having particular defined properties, both structural and biological.

Various cDNAs encoding these molecules were obtained from primate, e.g., human, and/or rodent, e.g., mouse, cDNA sequence libraries. Other primate or other mammalian counterparts would also be desired.

Some of the standard methods applicable are described or referenced, e.g., in  
 5 Maniatis, et al. (1982) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor Press; Sambrook, et al. (1989) Molecular Cloning: A Laboratory Manual, (2d ed.), vols. 1-3, CSH Press, NY; Ausubel, et al., Biology, Greene Publishing Associates, Brooklyn, NY; or Ausubel, et al. (1987 and periodic supplements) Current Protocols in Molecular Biology, Greene/Wiley, New York; each of which is  
 10 incorporated herein by reference.

Nucleotide (SEQ ID NO: 1) and corresponding amino acid sequence (SEQ ID NO: 2) of a primate, e.g., human, DCRS6 coding segment is shown in Table 1 along with reverse translation (SEQ ID NO: 3). Rodent, e.g., mouse, counterpart sequences are provided, e.g., SEQ ID NO: 4-6.

15 Similarly, nucleotide (SEQ ID NO: 7) and corresponding amino acid sequence (SEQ ID NO: 8) of a primate, e.g., human, DCRS7 coding segment is shown in Table 2 along with reverse translation (SEQ ID NO: 9). Rodent, e.g., mouse, counterpart sequences are provided, e.g., SEQ ID NO: 10-12. Nucleotide (SEQ ID NO: 13) and corresponding amino acid sequence (SEQ ID NO: 14) of a primate, e.g., human, DCRS8  
 20 coding segment is shown in Table 3 along with reverse translation (SEQ ID NO: 15).

Nucleotide (SEQ ID NO: 16) and corresponding amino acid sequence (SEQ ID NO: 17) of a primate, e.g., human, DCRS9 coding segment is shown in Table 4 along with reverse translation (SEQ ID NO: 18). Rodent, e.g., mouse, counterpart sequences are provided, e.g., SEQ ID NO: 19-21. Nucleotide (SEQ ID NO: 22) and corresponding  
 25 amino acid sequence (SEQ ID NO: 23) of a primate, e.g., human, DCRS10 coding segment is shown in Table 5 along with reverse translation (SEQ ID NO: 24). Rodent, e.g., mouse, counterpart sequences are provided, e.g., SEQ ID NO: 26-27.

30 Table 1: Nucleotide and polypeptide sequences of DNAX Cytokine Receptor Subunit like embodiments (DCRS6). Primate, e.g., human, embodiment (see SEQ ID NO: 1 and 2). Predicted signal sequence indicated, but may vary by a few positions and depending upon cell type.

35	gcg atg tgc ctc gtg ctg cta agc ctg gcc gcg ctg tgc agg agc gcc	48
	Met Ser Leu Val Leu Leu Ser Leu Ala Ala Leu Cys Arg Ser Ala	
	-10 -5 -1 1	
40	gta ccc cga gag ccg acc gtt caa tgt ggc tct gaa act ggg cca tct	96
	Val Pro Arg Glu Pro Thr Val Gln Cys Gly Ser Glu Thr Gly Pro Ser	
	5 10 15	

	cca gag tgg atg cta caa cat gat cta atc ccg gga gac ttg agg gac	144
	Pro Glu Trp Met Leu Gln His Asp Leu Ile Pro Gly Asp Leu Arg Asp	
	20 25 30	
5	ctc cga gta gaa cct gtt aca act agt gtt gca aca ggg gac tat tca	192
	Leu Arg Val Glu Pro Val Thr Thr Ser Val Ala Thr Gly Asp Tyr Ser	
	35 40 45	
10	att ttg atg aat gta agc tgg gta ctc cgg gca gat gcc agc atc cgc	240
	Ile Leu Met Asn Val Ser Trp Val Leu Arg Ala Asp Ala Ser Ile Arg	
	50 55 60 65	
15	ttg ttg aag gcc acc aag att tgt gtg acg ggc aaa agc aac ttc cag	288
	Leu Leu Lys Ala Thr Lys Ile Cys Val Thr Gly Lys Ser Asn Phe Gln	
	70 75 80	
20	tcc tac agc tgt gtg agg tgc aat tac aca gag gcc ttc cag act cag	336
	Ser Tyr Ser Cys Val Arg Cys Asn Tyr Thr Glu Ala Phe Gln Thr Gln	
	85 90 95	
	acc aga ccc tct ggt ggt aaa tgg aca ttt tcc tat atc ggc ttc cct	384
	Thr Arg Pro Ser Gly Gly Lys Trp Thr Phe Ser Tyr Ile Gly Phe Pro	
	100 105 110	
25	gta gag ctg aac aca gtc tat ttc att ggg gcc cat aat att cct aat	432
	Val Glu Leu Asn Thr Val Tyr Phe Ile Gly Ala His Asn Ile Pro Asn	
	115 120 125	
30	gca aat atg aat gaa gat ggc cct tcc atg tct gtg aat ttc acc tca	480
	Ala Asn Met Asn Glu Asp Gly Pro Ser Met Ser Val Asn Phe Thr Ser	
	130 135 140 145	
35	cca ggc tgc cta gac cac ata atg aaa tat aaa aaa aag tgt gtc aag	528
	Pro Gly Cys Leu Asp His Ile Met Lys Tyr Lys Lys Lys Cys Val Lys	
	150 155 160	
40	gcc gga agc ctg tgg gat ccg aac atc act gct tgt aag aag aat gag	576
	Ala Gly Ser Leu Trp Asp Pro Asn Ile Thr Ala Cys Lys Lys Asn Glu	
	165 170 175	
	gag aca gta gaa gtg aac ttc aca acc act ccc ctg gga aac aga tac	624
	Glu Thr Val Glu Val Asn Phe Thr Thr Thr Pro Leu Gly Asn Arg Tyr	
	180 185 190	
45	atg gct ctt atc caa cac agc act atc atc ggg ttt tct cag gtg ttt	672
	Met Ala Leu Ile Gln His Ser Thr Ile Ile Gly Phe Ser Gln Val Phe	
	195 200 205	
50	gag cca cac cag aag aaa caa acg cga gct tca gtg gtg att cca gtg	720
	Glu Pro His Gln Lys Lys Gln Thr Arg Ala Ser Val Val Ile Pro Val	
	210 215 220 225	
55	act ggg gat agt gaa ggt gct acg gtg cag ctg act cca tat ttt cct	768
	Thr Gly Asp Ser Glu Gly Ala Thr Val Gln Leu Thr Pro Tyr Phe Pro	
	230 235 240	

	act tgt ggc agc gac tgc atc cga cat aaa gga aca gtt gtg ctc tgc	816
	Thr Cys Gly Ser Asp Cys Ile Arg His Lys Gly Thr Val Val Leu Cys	
	245 250 255	
5	cca caa aca ggc gtc cct ttc cct ctg gat aac aac aaa agc aag ccg	864
	Pro Gln Thr Gly Val Pro Phe Pro Leu Asp Asn Asn Lys Ser Lys Pro	
	260 265 270	
10	gga ggc tgg ctg cct ctc ctc ctg ctg tct ctg ctg gtg gcc aca tgg	912
	Gly Gly Trp Leu Pro Leu Leu Leu Leu Ser Leu Leu Val Ala Thr Trp	
	275 280 285	
15	gtg ctg gtg gca ggg atc tat cta atg tgg agg cac gaa agg atc aag	960
	Val Leu Val Ala Gly Ile Tyr Leu Met Trp Arg His Glu Arg Ile Lys	
	290 295 300 305	
20	aag act tcc ttt tct acc acc aca cta ctg ccc ccc att aag gtt ctt	1008
	Lys Thr Ser Phe Ser Thr Thr Thr Leu Leu Pro Pro Ile Lys Val Leu	
	310 315 320	
	gtg gtt tac cca tct gaa ata tgt ttc cat cac aca att tgt tac ttc	1056
	Val Val Tyr Pro Ser Glu Ile Cys Phe His His Thr Ile Cys Tyr Phe	
	325 330 335	
25	act gaa ttt ctt caa aac cat tgc aga agt gag gtc atc ctt gaa aag	1104
	Thr Glu Phe Leu Gln Asn His Cys Arg Ser Glu Val Ile Leu Glu Lys	
	340 345 350	
30	tgg cag aaa aag aaa ata gca gag atg ggt cca gtg cag tgg ctt gcc	1152
	Trp Gln Lys Lys Lys Ile Ala Glu Met Gly Pro Val Gln Trp Leu Ala	
	355 360 365	
35	act caa aag aag gca gca gac aaa gtc gtc ttc ctt ctt tcc aat gac	1200
	Thr Gln Lys Lys Ala Ala Asp Lys Val Val Phe Leu Leu Ser Asn Asp	
	370 375 380 385	
40	gtc aac agt gtg tgc gat ggt acc tgt ggc aag agc gag ggc agt ccc	1248
	Val Asn Ser Val Cys Asp Gly Thr Cys Gly Lys Ser Glu Gly Ser Pro	
	390 395 400	
	agt gag aac tct caa gac ctc ttc ccc ctt gcc ttt aac ctt ttc tgc	1296
	Ser Glu Asn Ser Gln Asp Leu Phe Pro Leu Ala Phe Asn Leu Phe Cys	
	405 410 415	
45	agt gat cta aga agc cag att cat ctg cac aaa tac gtg gtg gtc tac	1344
	Ser Asp Leu Arg Ser Gln Ile His Leu His Lys Tyr Val Val Val Tyr	
	420 425 430	
50	ttt aga gag att gat aca aaa gac gat tac aat gct ctc agt gtc tgc	1392
	Phe Arg Glu Ile Asp Thr Lys Asp Asp Tyr Asn Ala Leu Ser Val Cys	
	435 440 445	
55	ccc aag tac cac ctc atg aag gat gcc act gct ttc tgt gca gaa ctt	1440
	Pro Lys Tyr His Leu Met Lys Asp Ala Thr Ala Phe Cys Ala Glu Leu	
	450 455 460 465	

	ctc cat gtc aag cag cag gtg tca gca gga aaa aga tca caa gcc tgc	1488
	Leu His Val Lys Gln Gln Val Ser Ala Gly Lys Arg Ser Gln Ala Cys	
	470 475 480	
5	cac gat ggc tgc tgc tcc ttg tagccacccc atgagaagca agagacctta	1539
	His Asp Gly Cys Cys Ser Leu	
	485	
10	aaggcttctt atcccaccaa ttacagggaa aaaacgtgtg atgatcctga agcttactat	1599
	gcagcctaca aacagcctta gtaattaaaa cattttatac caataaaatt ttcaaattatt	1659
	gctaactaat gtagcattaa ctaacgattg gaaactacat ttacaacttc aaagctgttt	1719
15	tatacataga aatcaattac agctttaatt gaaaactgta accatthttga taatgcaaca	1779
	ataaagcatc ttcagcc	1796
20	MSLVLLSLAALCRSAVPREPTVQCGSETGPSPEWMLQHDLLIPGDLRLDLRVEPVTTSVATGDYSILMNVSWVL	
	RADASIRLLKATKICVTGKSNFQSYSCVRCNYTEAFQTQTRPSGGKWTFSYIGFPVELNTVYFIGAHNIPNA	
	NMNEDGPSMSVNFTSPGCLDHIMKYKKKCVKAGSLWDPNITACKNREETVEVNFTTTPLGNRYMALIQHSTI	
	IGFSQVFEPHQKKQTRASVVIPTVGDSEGATVQLTPYFPTCGSDCIRHKGTVVLCPTGVPFPLDNNKSKPG	
	GWLPLLLLSLLVATWVLVAGIYLMWRHERIKTSFSTTTLLPPIKVLVVYPSEICFHHTICYFTEFLQNHCR	
25	SEVILEKWQKKKIAEMGPVQWLATQKKAADKVVFLSNDVNSVCDGTCGKSEGPSSENSQDLFPLAFNLFCS	
	DLRSQIHLHKYVVVVFREIDTKDDYNALSVC PKYHLMKDATAFCAELLHVKOOVSAGKRSOACHDGCCSL.	

Reverse translation of primate, e.g., human, DCRS6 (SEQ ID NO: 3):

30	atgwsnytnng	tnytnytnws	nytnngcngcn	ytntgymgnw	sngcngtncc	nmngnarcen	60
	acngtncart	gyggngwsnga	racnggnccn	wsncngart	ggatgytnca	rcaygayytn	120
	athccngng	ayytnmgnga	yytnmgngtn	garccngtna	cnacnwsngt	ngcnacnggn	180
35	gaytaywsna	thytnatgaa	ygtnwsntgg	gtnytnmgng	cngaygcnws	nathmgnytn	240
	ytnaargcna	cnaarathtg	ygtnacnggn	aarwsnaayt	tycarwsnta	ywsntgygtn	300
40	mgntgyaayt	ayacngargc	nttycaracn	caracnmgnc	cnwsnggngg	naartggacn	360
	ttywsntaya	thggnttycc	ngtngarytn	aayacngtnt	ayttyathgg	ngcncayaay	420
	athccnaayg	cnaayatgaa	ygargaygg	ccnwsnatgw	sngtnaaytt	yacnwsnccn	480
45	ggntgyytng	aycayathat	gaartayaar	aaraartgyg	tnaargcngg	nwsnytnntgg	540
	gayccnaaya	thacngcntg	yaaraaraay	gargaracng	tn gargtnaa	yttyacnacn	600
50	acnccnytnng	gnaaymgnta	yatggcnytn	athcarcayw	snacnathat	hggnttywsn	660
	cargtnnttyg	arcncayca	raaraarcar	acnmngncnw	sngtngtntat	hccngtnacn	720
	ggngaywsng	arggngcnac	ngtnrcarytn	acnccntayt	tyccnacntg	yggngwsngay	780
55	tgyathmgnc	ayaarggnac	ngtngtnytn	tgyccncara	cnggngtncc	nttyccnytn	840
	gayaayaaya	arwsnaarcc	ngngngntgg	ytncnytnny	tnytnytnws	nytnytnngtn	900

gcnacntggg tnytngtngc nggnathtay ytnatgtggm gncaygarmg nathaaraar 960  
 5 acnwsnttyw snacnacnac nytnytnccn ccnathaarg tnytngtngt ntayccnwsn 1020  
 garathtgyt tycaycayac nathtgytay ttyacngart tyytncaraa ycaytgymgn 1080  
 wsnrgargtna thytngaraa rtggcaraar aaraarathg cngaratggg nccngtncar 1140  
 10 tggytngcna cncaraaraa rgcngcngay aargtngtnt tyytnytnws naaygaygtn 1200  
 aaywsngtnt gygaygnac ntgyggnaar wsnrgaggw snccnwsnga raaywsncar 1260  
 15 gayytnttyc cnytngcntt yaayytntty tgywsngayy tnmgnwsnca rathcayytn 1320  
 cayaartayg tngtngtnta yttymngar athgayacna argaygayta yaaygcnytn 1380  
 wsngtntgyt cnaartayca yytnatgaar gaygcnacng cnttytgygc ngarytnytn 1440  
 20 caygtnaarc arcargtnws ngcnggnaar mgnwsncarg cntgycayga yggntgytgy 1500  
 wsnytn 1506

25 Rodent, e.g., mouse embodiment (see SEQ ID NO: 4 and 5).

gat ttc agc agc cag acg cat ctg cac aaa tac ctg gag gtc tat ctt 48  
 Asp Phe Ser Ser Gln Thr His Leu His Lys Tyr Leu Glu Val Tyr Leu  
 1 5 10 15  
 30 ggg gga gca gac ctc aaa ggc gac tat aat gcc ctg agt gtc tgc ccc 96  
 Gly Gly Ala Asp Leu Lys Gly Asp Tyr Asn Ala Leu Ser Val Cys Pro  
 20 25 30  
 35 caa tat cat ctc atg aag gac gcc aca gct ttc cac aca gaa ctt ctc 144  
 Gln Tyr His Leu Met Lys Asp Ala Thr Ala Phe His Thr Glu Leu Leu  
 35 40 45  
 40 aag gct acg cag agc atg tca gtg aag aaa cgc tca caa gcc tgc cat 192  
 Lys Ala Thr Gln Ser Met Ser Val Lys Lys Arg Ser Gln Ala Cys His  
 50 55 60  
 gat agc tgt tca ccc ttg tagtccaccc gggggaatag agactctgaa 240  
 45 Asp Ser Cys Ser Pro Leu  
 65 70  
 gccttcctac tctcccttcc agtgacaaat gctgtgtgac gactctgaaa tgtgtgggag 300  
 aggctgtgtg gaggtagtgc tatgtacaaa cttgctttaa aactggagtt tgcaaagtca 360  
 50 acctgagcat acacgcctga ggctagtcat tggctggatt tatgaagaca acacagttac 420  
 agacaataat gagtgggacc tacatttggg atatacccaa agctgggtaa tgattatcac 480  
 55 tgagaaccac gcactctggc catgaggtaa tacggcactt ccctgtcagg ctgtctgtca 540  
 gggtgggtct gtcttgact gcccatgctc tatgctgcac gtagaccgtt ttgtaacatt 600  
 ttaatctgtt aatgaataat ccgtttggga ggctctc 637



DFSSQTHLHKYLEVYLGGADLKG DYNALSVCPQYHLMKDATAFHTELLKATQSMSVKKRSQACHDSCSPL.

5 Reverse translation of rodent, e.g., mouse, DCRS6 (SEQ ID NO: 6):

gayttywsnw sncaracnca yytncayaar tayytnngarg tntayytnng ngngncngay 60  
 ytnaarggng aytayaaygc nytnwsngtn tgyccncart aycayytnat gaargaygcn 120  
 10 acngcnttyc ayacngaryt nytnaargcn acncarwsna tgwsngtnaa raarmgnwsn 180  
 cargcntgyc aygaywsntg ywsnccnytn 210

15

Table 2: Nucleotide and polypeptide sequences of DNAX Cytokine Receptor Subunit like  
 embodiments (DCRS7). Primate, e.g., human, embodiment (see SEQ ID NO: 7 and 8).  
 Predicted signal sequence indicated, but may vary by a few positions and depending upon cell  
 type.

20

gagtcaggac tcccaggaca gagagtgcac aaactaccca gcacagcccc ctccgcccc 60

tctggagggt gaagagggat tccagcccct gccaccacaca gacacggggt gactgggggtg 120

25

tctgcccccc ttggggggcan ccacaggggcc tcaggcctgg gtgccacctg gcactagaag 180

atg cct gtg ccc tgg ttc ttg ctg tcc ttg gca ctg ggc cga agc cag 228  
 Met Pro Val Pro Trp Phe Leu Leu Ser Leu Ala Leu Gly Arg Ser Gln  
 -20 -15 -10 -5

30

tgg atc ctt tct ctg gag agg ctt gtg ggg cct cag gac gct acc cac 276  
 Trp Ile Leu Ser Leu Glu Arg Leu Val Gly Pro Gln Asp Ala Thr His  
 -1 1 5 10

35

tgc tct ccg ggc ctc tcc tgc cgc ctc tgg gac agt gac ata ctc tgc 324  
 Cys Ser Pro Gly Leu Ser Cys Arg Leu Trp Asp Ser Asp Ile Leu Cys  
 15 20 25

40

ctg cct ggg gac atc gtg cct gct ccg ggc ccc gtg ctg gcg cct acg 372  
 Leu Pro Gly Asp Ile Val Pro Ala Pro Gly Pro Val Leu Ala Pro Thr  
 30 35 40

45

cac ctg cag aca gag ctg gtg ctg agg tgc cag aag gag acc gac tgt 420  
 His Leu Gln Thr Glu Leu Val Leu Arg Cys Gln Lys Glu Thr Asp Cys  
 45 50 55 60

50

gac ctc tgt ctg cgt gtg gct gtc cac ttg gcc gtg cat ggg cac tgg 468  
 Asp Leu Cys Leu Arg Val Ala Val His Leu Ala Val His Gly His Trp  
 65 70 75

gaa gag cct gaa gat gag gaa aag ttt gga gga gca gct gac tta ggg 516  
 Glu Glu Pro Glu Asp Glu Glu Lys Phe Gly Gly Ala Ala Asp Leu Gly  
 80 85 90

55

gtg gag gag cct agg aat gcc tct ctc cag gcc caa gtc gtg ctc tcc 564  
 Val Glu Glu Pro Arg Asn Ala Ser Leu Gln Ala Gln Val Val Leu Ser  
 95 100 105

	ttc cag gcc tac cct act gcc cgc tgc gtc ctg ctg gag gtg caa gtg	612
	Phe Gln Ala Tyr Pro Thr Ala Arg Cys Val Leu Leu Glu Val Gln Val	
	110 115 120	
5	cct gct gcc ctt gtg cag ttt ggt cag tct gtg ggc tct gtg gta tat	660
	Pro Ala Ala Leu Val Gln Phe Gly Gln Ser Val Gly Ser Val Val Tyr	
	125 130 135 140	
10	gac tgc ttc gag gct gcc cta ggg agt gag gta cga atc tgg tcc tat	708
	Asp Cys Phe Glu Ala Ala Leu Gly Ser Glu Val Arg Ile Trp Ser Tyr	
	145 150 155	
15	act cag ccc agg tac gag aag gaa ctc aac cac aca cag cag ctg cct	756
	Thr Gln Pro Arg Tyr Glu Lys Glu Leu Asn His Thr Gln Gln Leu Pro	
	160 165 170	
20	gac tgc agg ggg ctc gaa gtc tgg aac agc atc ccg agc tgc tgg gcc	804
	Asp Cys Arg Gly Leu Glu Val Trp Asn Ser Ile Pro Ser Cys Trp Ala	
	175 180 185	
25	ctg ccc tgg ctc aac gtg tca gca gat ggt gac aac gtg cat ctg gtt	852
	Leu Pro Trp Leu Asn Val Ser Ala Asp Gly Asp Asn Val His Leu Val	
	190 195 200	
30	ctg aat gtc tct gag gag cag cac ttc ggc ctc tcc ctg tac tgg aat	900
	Leu Asn Val Ser Glu Glu Gln His Phe Gly Leu Ser Leu Tyr Trp Asn	
	205 210 215 220	
35	cag gtc cag ggc ccc cca aaa ccc cgg tgg cac aaa aac ctg act gga	948
	Gln Val Gln Gly Pro Pro Lys Pro Arg Trp His Lys Asn Leu Thr Gly	
	225 230 235	
40	ccg cag atc att acc ttg aac cac aca gac ctg gtt ccc tgc ctc tgt	996
	Pro Gln Ile Ile Thr Leu Asn His Thr Asp Leu Val Pro Cys Leu Cys	
	240 245 250	
45	att cag gtg tgg cct ctg gaa cct gac tcc gtt agg acg aac atc tgc	1044
	Ile Gln Val Trp Pro Leu Glu Pro Asp Ser Val Arg Thr Asn Ile Cys	
	255 260 265	
50	ccc ttc agg gag gac ccc cgc gca cac cag aac ctc tgg caa gcc gcc	1092
	Pro Phe Arg Glu Asp Pro Arg Ala His Gln Asn Leu Trp Gln Ala Ala	
	270 275 280	
55	cga ctg cga ctg ctg acc ctg cag agc tgg ctg ctg gac gca ccg tgc	1140
	Arg Leu Arg Leu Leu Thr Leu Gln Ser Trp Leu Leu Asp Ala Pro Cys	
	285 290 295 300	
60	tgc ctg ccc gca gaa gcg gca ctg tgc tgg cgg gct ccg ggt ggg gac	1188
	Ser Leu Pro Ala Glu Ala Ala Leu Cys Trp Arg Ala Pro Gly Gly Asp	
	305 310 315	
65	ccc tgc cag cca ctg gtc cca ccg ctt tcc tgg gag aat gtc act gtg	1236
	Pro Cys Gln Pro Leu Val Pro Pro Leu Ser Trp Glu Asn Val Thr Val	
	320 325 330	
70	gac gtg aac agc tcg gag aag ctg cag ctg cag gag tgc ttg tgg gct	1284
	Asp Val Asn Ser Ser Glu Lys Leu Gln Leu Gln Glu Cys Leu Trp Ala	
	335 340 345	

5	gac tcc ctg ggg cct ctc aaa gac gat gtg cta ctg ttg gag aca cga 1332															
	Asp Ser Leu Gly Pro Leu Lys Asp Asp Val Leu Leu Leu Glu Thr Arg	350				355					360					
10	ggc ccc cag gac aac aga tcc ctc tgt gcc ttg gaa ccc agt ggc tgt 1380															
	Gly Pro Gln Asp Asn Arg Ser Leu Cys Ala Leu Glu Pro Ser Gly Cys	365			370				375					380		
15	act tca cta ccc agc aaa gcc tcc acg agg gca gct cgc ctt gga gag 1428															
	Thr Ser Leu Pro Ser Lys Ala Ser Thr Arg Ala Ala Arg Leu Gly Glu			385				390						395		
20	tac tta cta caa gac ctg cag tca ggc cag tgt ctg cag cta tgg gac 1476															
	Tyr Leu Leu Gln Asp Leu Gln Ser Gly Gln Cys Leu Gln Leu Trp Asp		400				405						410			
25	gat gac ttg gga gcg cta tgg gcc tgc ccc atg gac aaa tac atc cac 1524															
	Asp Asp Leu Gly Ala Leu Trp Ala Cys Pro Met Asp Lys Tyr Ile His	415				420						425				
30	aag cgc tgg gcc ctc gtg tgg ctg gcc tgc cta ctc ttt gcc gct gcg 1572															
	Lys Arg Trp Ala Leu Val Trp Leu Ala Cys Leu Leu Phe Ala Ala Ala	430				435					440					
35	ctt tcc ctc atc ctc ctt ctc aaa aag gat cac gcg aaa ggg tgg ctg 1620															
	Leu Ser Leu Ile Leu Leu Leu Lys Lys Asp His Ala Lys Gly Trp Leu	445			450				455					460		
40	agg ctc ttg aaa cag gac gtc cgc tcg ggg gcg gcc gcc agg ggc cgc 1668															
	Arg Leu Leu Lys Gln Asp Val Arg Ser Gly Ala Ala Ala Arg Gly Arg			465				470						475		
45	gcg gct ctg ctc ctc tac tca gcc gat gac tcg ggt ttc gag cgc ctg 1716															
	Ala Ala Leu Leu Leu Tyr Ser Ala Asp Asp Ser Gly Phe Glu Arg Leu		480				485						490			
50	gtg ggc gcc ctg gcg tcg gcc ctg tgc cag ctg ccg ctg cgc gtg gcc 1764															
	Val Gly Ala Leu Ala Ser Ala Leu Cys Gln Leu Pro Leu Arg Val Ala	495				500						505				
55	gta gac ctg tgg agc cgt cgt gaa ctg agc gcg cag ggg ccc gtg gct 1812															
	Val Asp Leu Trp Ser Arg Arg Glu Leu Ser Ala Gln Gly Pro Val Ala	510				515					520					
60	tgg ttt cac gcg cag cgg cgc cag acc ctg cag gag ggc ggc gtg gtg 1860															
	Trp Phe His Ala Gln Arg Arg Gln Thr Leu Gln Glu Gly Gly Val Val	525				530				535				540		
65	gtc ttg ctc ttc tct ccc ggt gcg gtg gcg ctg tgc agc gag tgg cta 1908															
	Val Leu Leu Phe Ser Pro Gly Ala Val Ala Leu Cys Ser Glu Trp Leu			545				550						555		
70	cag gat ggg gtg tcc ggg ccc ggg gcg cac ggc ccg cac gac gcc ttc 1956															
	Gln Asp Gly Val Ser Gly Pro Gly Ala His Gly Pro His Asp Ala Phe		560				565						570			

	cgc gcc tcg ctc agc tgc gtg ctg ccc gac ttc ttg cag ggc cgg gcg	2004
	Arg Ala Ser Leu Ser Cys Val Leu Pro Asp Phe Leu Gln Gly Arg Ala	
	575 580 585	
5	ccc ggc agc tac gtg ggg gcc tgc ttc gac agg ctg ctc cac ccg gac	2052
	Pro Gly Ser Tyr Val Gly Ala Cys Phe Asp Arg Leu Leu His Pro Asp	
	590 595 600	
10	gcc gta ccc gcc ctt ttc cgc acc gtg ccc gtc ttc aca ctg ccc tcc	2100
	Ala Val Pro Ala Leu Phe Arg Thr Val Pro Val Phe Thr Leu Pro Ser	
	605 610 615 620	
15	caa ctg cca gac ttc ctg ggg gcc ctg cag cag cct cgc gcc ccg cgt	2148
	Gln Leu Pro Asp Phe Leu Gly Ala Leu Gln Gln Pro Arg Ala Pro Arg	
	625 630 635	
20	tcc ggg cgg ctc caa gag aga gcg gag caa gtg tcc cgg gcc ctt cag	2196
	Ser Gly Arg Leu Gln Glu Arg Ala Glu Gln Val Ser Arg Ala Leu Gln	
	640 645 650	
25	cca gcc ctg gat agc tac ttc cat ccc ccg ggg acn tcc gcg ccg gga	2244
	Pro Ala Leu Asp Ser Tyr Phe His Pro Pro Gly Xaa Ser Ala Pro Gly	
	655 660 665	
30	cgc ggg gtg gga cca ggg gcg gga cct ggg gcg ggg gac ggg act	2289
	Arg Gly Val Gly Pro Gly Ala Gly Pro Gly Ala Gly Asp Gly Thr	
	670 675 680	
35	taaataaaagg cagacgctg	2308
40	MPVPWFLLSLALGRSQWILSLERLVGPQDATHCSPGLSCRLWDSILCLPGDIVPAPGPVLAPTHLQTELVL RCQKETDCDLCLRVAVHLAVHGHWEPEDEEKFGGAADLGVEEPRNASLQAQVVLSPQAYPTARCVLLEVVQV PAALVQFGQSVGSVVYDCFEAALGSEVRIWSYTPRYEKELNHTQQLPDCRGLEVWNSIPSCWALPWLNVSA DGDNVHLVLNVSEEQHFGLSLYWNQVQGPPKPRWHKNLTGPGQIITLNHTDLVPCLCIQVWPLEPDSVRTNIC PFREDPRAHQNLWQAARLRLTLTQSWLLDAPCSLPAAEALCWRAPGGDPQPLVPPLSWENVTVDVNSSEKL QLQECLEWADSLGPLKDDVLLLETRGPQDNRSLEPSGCTSLPSKASTRAARLGEYLLQDLQSGQCLQLWD DDLGALWACPMCKYIHKRWALVWLACLLFAAALSLILLLKKDHAKGWLRLKQDVRSGAAARGRAALLLYSA DDSGFERLVGALASALCQLPLRVAVDLWSRRELSAQGPVAFWFAHQRRQTLQEGGVVLLFSPGAVALCSEWL QDGVSGPGAHGPHDAFRASLSCVLPDFLQGRAPGSYVGACFDRLHLPDAVPALFRTVPVFTLPSQLPDLFLGA LQQPRAPRSGRLQERAEQVSRALQPALDSYFHPPGTSAPGRGVGPGAGPGAGDGT.	

Reverse translation of primate, e.g., human, DCRS7 (SEQ ID NO: 9):

45	atgccngtnc cntggttyyt nytnwsnytn gcnytnggnm gnwsncartg gathytnwnsn	60
	ytngarmgny tngtnggncc ncargaygc acncaytgyw snccnggnyt nwsntgymgn	120
50	ytntgggayw sngayathyt ntgyytnccn ggngayathg tncngcncc nggnccngtn	180
	ytngcnccna cncayytnca racngarytn gtntytnmgt gycaraarga racngaytgy	240
	gayytnygyy tnmngntngc ngtncayytn gcngtncayg gncaytggga rgarcncgar	300
55	gaygargara arttyggngg ngcngcngay ytngngntng argarcnmg naaygcwnsn	360
	ytncargenc argtngntyt nwsnttycar gentayccna cngcnmngtg ygtnytnytn	420
	gargtnarg tncngcngc nytngtncar ttyggncarw sngtnggnws ngtngtntay	480

5      gaytgyttyg argcngcnyt nggnwsngar gtnmgnatht ggwsntayac ncarccnmgn 540  
 taygaraarg arytnaayca yacncarcar ytnccngayt gymgnggnyt ngargtntgg 600  
 aaywsnathc cnwsntgytg ggcnynccn tggynaaayg tnwsngcnga yggngayaay 660  
 gtncayytng tnytnaaygt nwsngargar carcayttyg gnytnwsnyt ntaytggaay 720  
 10      cargtncarg gncncncaa rccnmgttg cayaaraayy tnacnggncc ncarathath 780  
 acnytnaayc ayacngayyt ngtnccntgy ytntgyathc argtntggcc nytngarccn 840  
 15      gaywsngtnm gnacnaayat htgyccntty mgngargayc cnmgngcnca ycaraaaytn 900  
 tggcargcng cnmgnytmg nytnytnacn ytnrcarwsnt ggytnytnga ygcncntgy 960  
 wsnytnccng cngargcngc nytnrgygtg mgngcncng gngngaycc ntgycarccn 1020  
 20      ytngtnccnc cnytnwsntg ggaraaygt acngtngayg tnaaywsnws ngaraarytn 1080  
 carytncarg artgyytntg ggcngaywsn ytnggncny tnaargayga ygtnytntn 1140  
 ytngaracnm gnggncnca rgayaaymgn wsnytnrgy cnytngarcc nwsnggntgy 1200  
 25      acnwsnytn cnsnaargc nwsnacnmgn gcngcnmgy tngngarta yytnytncar 1260  
 gayytnrcarw snggncartg yytnrcarytn tgggagayg ayytnggngc nytnrggcn 1320  
 30      tgyccnatgg ayaartayat hcayaarmgn tgggcnytng tntggytngc ntgyytnytnt 1380  
 ttygcngcng cnytnwsnyt nathytnytnt ytnaaraarg aycaygnaa rggntggytn 1440  
 35      mgnytntna arcargaygt nmgnwsnggn gcngcngcnm gnggnmgngc ngcnytnytnt 1500  
 ytntaywsng cngaygayws nggnttygar mgnytngtng gngcnytnge nwsngcnytn 1560  
 tgyrcarytn cnytnmgngt ngngtngay ytntggwsnm gnmngaryt nwsngcncar 1620  
 40      ggncngtng cntggtyca ygcncarmgn mgncaracny tncargargg ngngtngtn 1680  
 gtnytntnt tywsnccng ngcngtngcn ytntgywsng artggytnca rgayggngtn 1740  
 45      wsnggncng gngcncaygg nccncaygay gcnttymng cnsnytnws ntgygtnytnt 1800  
 ccngayttyt tncarggmng ngcncnggn wsntaygtng gngcntgytt ygaymgnytnt 1860  
 ytncaycng aygcngtncc ngcnytnntt mgnacngtnc cngnttyac nytnccnwsn 1920  
 50      carytnccng aytyytngg ngcnytnrcar carccnmng cncnmgnws nggnmgnytnt 1980  
 cargarmng cngarcargt nwsnmngcn ytnrcarccng cnytngayws ntayttyay 2040  
 55      ccncnggna cnsngcncc nggnmgnggn gtnggncng gngcngncc ngngcnggn 2100  
 gayggnacn 2109

Rodent, e.g., mouse, embodiment (see SEQ ID NO: 10 and 11). Predicted signal sequence indicated, but may vary by a few positions and depending upon cell type.

5	ccaaatcgaa agcacgggag ctgatactgg gcctggagtc caggctcact ggagtgggga	60
	agcatggctg gagaggaatt ctagcccttg ctctctccca gggacacggg gctgattgtc	120
	agcaggggcg aggggtctgc ccccccttgg gggggcagga cggggcctca ggcctgggtg	180
10	ctgtccggca cctggaag atg cct gtg tcc tgg ttc ctg ctg tcc ttg gca	231
	Met Pro Val Ser Trp Phe Leu Leu Ser Leu Ala	
	-20 -15 -10	
15	ctg ggc cga aac cct gtg gtc gtc tct ctg gag aga ctg atg gag cct	279
	Leu Gly Arg Asn Pro Val Val Val Ser Leu Glu Arg Leu Met Glu Pro	
	-5 -1 1 5	
20	cag gac act gca cgc tgc tct cta ggc ctc tcc tgc cac ctc tgg gat	327
	Gln Asp Thr Ala Arg Cys Ser Leu Gly Leu Ser Cys His Leu Trp Asp	
	10 15 20	
25	ggt gac gtg ctc tgc ctg cct gga agc ctc cag tct gcc cca ggc cct	375
	Gly Asp Val Leu Cys Leu Pro Gly Ser Leu Gln Ser Ala Pro Gly Pro	
	25 30 35	
30	gtg cta gtg cct acc cgc ctg cag acg gag ctg gtg ctg agg tgt cca	423
	Val Leu Val Pro Thr Arg Leu Gln Thr Glu Leu Val Leu Arg Cys Pro	
	40 45 50 55	
35	cag aag aca gat tgc gcc ctc tgt gtc cgt gtg gtg gtc cac ttg gcc	471
	Gln Lys Thr Asp Cys Ala Leu Cys Val Arg Val Val Val His Leu Ala	
	60 65 70	
40	gtg cat ggg cac tgg gca gag cct gaa gaa gct gga aag tct gat tca	519
	Val His Gly His Trp Ala Glu Pro Glu Glu Ala Gly Lys Ser Asp Ser	
	75 80 85	
45	gaa ctc cag gag tct agg aac gcc tct ctc cag gcc cag gtg gtg ctc	567
	Glu Leu Gln Glu Ser Arg Asn Ala Ser Leu Gln Ala Gln Val Val Leu	
	90 95 100	
50	tcc ttc cag gcc tac ccc atc gcc cgc tgt gcc ctg ctg gag gtc cag	615
	Ser Phe Gln Ala Tyr Pro Ile Ala Arg Cys Ala Leu Leu Glu Val Gln	
	105 110 115	
55	gtg ccc gct gac ctg gtg cag cct ggt cag tcc gtg ggt tct gcg gta	663
	Val Pro Ala Asp Leu Val Gln Pro Gly Gln Ser Val Gly Ser Ala Val	
	120 125 130 135	
60	ttt gac tgt ttc gag gct agt ctt ggg gct gag gta cag atc tgg tcc	711
	Phe Asp Cys Phe Glu Ala Ser Leu Gly Ala Glu Val Gln Ile Trp Ser	
	140 145 150	
65	tac acg aag ccc agg tac cag aaa gag ctc aac ctc aca cag cag ctg	759
	Tyr Thr Lys Pro Arg Tyr Gln Lys Glu Leu Asn Leu Thr Gln Gln Leu	
	155 160 165	

	cct gac tgc agg ggt ctt gaa gtc cgg gac agc atc cag agc tgc tgg	807
	Pro Asp Cys Arg Gly Leu Glu Val Arg Asp Ser Ile Gln Ser Cys Trp	
	170 175 180	
5	gtc ctg ccc tgg ctc aat gtg tct aca gat ggt gac aat gtc ctt ctg	855
	Val Leu Pro Trp Leu Asn Val Ser Thr Asp Gly Asp Asn Val Leu Leu	
	185 190 195	
10	aca ctg gat gtc tct gag gag cag gac ttt agc ttc tta ctg tac ctg	903
	Thr Leu Asp Val Ser Glu Glu Gln Asp Phe Ser Phe Leu Leu Tyr Leu	
	200 205 210 215	
15	cgt cca gtc ccg gat gct ctc aaa tcc ttg tgg tac aaa aac ctg act	951
	Arg Pro Val Pro Asp Ala Leu Lys Ser Leu Trp Tyr Lys Asn Leu Thr	
	220 225 230	
20	gga cct cag aac att act tta aac cac aca gac ctg gtt ccc tgc ctc	999
	Gly Pro Gln Asn Ile Thr Leu Asn His Thr Asp Leu Val Pro Cys Leu	
	235 240 245	
	tgc att cag gtg tgg tgc cta gag cca gac tct gag agg gtc gaa ttc	1047
	Cys Ile Gln Val Trp Ser Leu Glu Pro Asp Ser Glu Arg Val Glu Phe	
	250 255 260	
25	tgc ccc ttc cgg gaa gat ccc ggt gca cac agg aac ctc tgg cac ata	1095
	Cys Pro Phe Arg Glu Asp Pro Gly Ala His Arg Asn Leu Trp His Ile	
	265 270 275	
30	gcc agg ctg cgg gta ctg tcc cca ggg gta tgg cag cta gat gcg cct	1143
	Ala Arg Leu Arg Val Leu Ser Pro Gly Val Trp Gln Leu Asp Ala Pro	
	280 285 290 295	
35	tgc tgt ctg ccg ggc aag gta aca ctg tgc tgg cag gca cca gac cag	1191
	Cys Cys Leu Pro Gly Lys Val Thr Leu Cys Trp Gln Ala Pro Asp Gln	
	300 305 310	
40	agt ccc tgc cag cca ctt gtg cca cca gtg ccc cag aag aac gcc act	1239
	Ser Pro Cys Gln Pro Leu Val Pro Pro Val Pro Gln Lys Asn Ala Thr	
	315 320 325	
	gtg aat gag cca caa gat ttc cag ttg gtg gca ggc cac ccc aac ctc	1287
	Val Asn Glu Pro Gln Asp Phe Gln Leu Val Ala Gly His Pro Asn Leu	
	330 335 340	
45	tgt gtc cag gtg agc acc tgg gag aag gtt cag ctg caa gcg tgc ttg	1335
	Cys Val Gln Val Ser Thr Trp Glu Lys Val Gln Leu Gln Ala Cys Leu	
	345 350 355	
50	tgg gct gac tcc ttg ggg ccc ttc aag gat gat atg ctg tta gtg gag	1383
	Trp Ala Asp Ser Leu Gly Pro Phe Lys Asp Asp Met Leu Leu Val Glu	
	360 365 370 375	
55	atg aaa acc ggc ctc aac aac aca tca gtc tgt gcc ttg gaa ccc agt	1431
	Met Lys Thr Gly Leu Asn Asn Thr Ser Val Cys Ala Leu Glu Pro Ser	
	380 385 390	
	ggc tgt aca cca ctg ccc agc atg gcc tcc acg aga gct gct cgc ctg	1479
	Gly Cys Thr Pro Leu Pro Ser Met Ala Ser Thr Arg Ala Ala Arg Leu	
	395 400 405	

5	gga gag gag ttg ctg caa gac ttc cga tca cac cag tgt atg cag ctg	1527
	Gly Glu Glu Leu Leu Gln Asp Phe Arg Ser His Gln Cys Met Gln Leu	
	410 415 420	
10	tgg aac gat gac aac atg gga tgc cta tgg gcc tgc ccc atg gac aag	1575
	Trp Asn Asp Asp Asn Met Gly Ser Leu Trp Ala Cys Pro Met Asp Lys	
	425 430 435	
15	tac atc cac agg cgc tgg gtc cta gta tgg ctg gcc tgc cta ctc ttg	1623
	Tyr Ile His Arg Arg Trp Val Leu Val Trp Leu Ala Cys Leu Leu Leu	
	440 445 450 455	
20	gct gcg gcg ctt ttc ttc ttc ctc ctt cta aaa aag gac cgc agg aaa	1671
	Ala Ala Ala Leu Phe Phe Phe Leu Leu Leu Lys Lys Asp Arg Arg Lys	
	460 465 470	
25	gcg gcc cgt ggc tcc cgc acg gcc ttg ctc ctc cac tcc gcc gac gga	1719
	Ala Ala Arg Gly Ser Arg Thr Ala Leu Leu Leu His Ser Ala Asp Gly	
	475 480 485	
30	gcg ggc tac gag cgc ctg gtg gga gca ctg gcg tcc gcg ttg agc cag	1767
	Ala Gly Tyr Glu Arg Leu Val Gly Ala Leu Ala Ser Ala Leu Ser Gln	
	490 495 500	
35	atg cca ctg cgc gtg gcc gtg gac ctg tgg agc cgc cgc gag ctg agc	1815
	Met Pro Leu Arg Val Ala Val Asp Leu Trp Ser Arg Arg Glu Leu Ser	
	505 510 515	
40	gcg cac gga gcc cta gcc tgg ttc cac cac cag cga cgc cgt atc ctg	1863
	Ala His Gly Ala Leu Ala Trp Phe His His Gln Arg Arg Arg Ile Leu	
	520 525 530 535	
45	cag gag ggt ggc gtg gta atc ctt ctc ttc tgc ccc gcg gcc gtg gcg	1911
	Gln Glu Gly Gly Val Val Ile Leu Leu Phe Ser Pro Ala Ala Val Ala	
	540 545 550	
50	cag tgt cag cag tgg ctg cag ctc cag aca gtg gag ccc ggg ccg cat	1959
	Gln Cys Gln Gln Trp Leu Gln Leu Gln Thr Val Glu Pro Gly Pro His	
	555 560 565	
55	gac gcc ctc gcc gcc tgg ctc agc tgc gtg cta ccc gat ttc ctg caa	2007
	Asp Ala Leu Ala Ala Trp Leu Ser Cys Val Leu Pro Asp Phe Leu Gln	
	570 575 580	
60	ggc cgg gcg acc ggc cgc tac gtc ggg gtc tac ttc gac ggg ctg ctg	2055
	Gly Arg Ala Thr Gly Arg Tyr Val Gly Val Tyr Phe Asp Gly Leu Leu	
	585 590 595	
65	cac cca gac tct gtg ccc tcc ccg ttc cgc gtc gcc ccg ctc ttc tcc	2103
	His Pro Asp Ser Val Pro Ser Pro Phe Arg Val Ala Pro Leu Phe Ser	
	600 605 610 615	
70	ctg ccc tgc cag ctg ccg gct ttc ctg gat gca ctg cag gga ggc tgc	2151
	Leu Pro Ser Gln Leu Pro Ala Phe Leu Asp Ala Leu Gln Gly Gly Cys	
	620 625 630	



tcc act tcc gcg ggg cga ccc gcg gac cgg gtg gaa cga gtg acc cag 2199  
 Ser Thr Ser Ala Gly Arg Pro Ala Asp Arg Val Glu Arg Val Thr Gln  
                   635                                  640                                  645

5      gcg ctg cgg tcc gcc ctg gac agc tgt act tct agc tcg gaa gcc cca 2247  
       Ala Leu Arg Ser Ala Leu Asp Ser Cys Thr Ser Ser Ser Glu Ala Pro  
                   650                                  655                                  660

10     ggc tgc tgc gag gaa tgg gac ctg gga ccc tgc act aca cta gaa 2292  
       Gly Cys Cys Glu Glu Trp Asp Leu Gly Pro Cys Thr Thr Leu Glu  
                   665                                  670                                  675

taaaagccga tacagtattc ct 2314

15     MPVSWFLLSLALGRNPVVVSLERLMEPQDTARCSLGLSCHLWDGDVLCPLPGSLQSAPGPVLPVTRLQTELVL  
       RCPQKTDCAICVRVVVHLAVHGHWAEPPEEAGKSDSELQESRNASLQAQVVLFSQAYPIARCALLEVQVPADL  
       VQPGQSVGSAVFDCFEASLGAEVQIWSYTKPRYQKELNLTQQLPDCRGLEVRDSIQSCWVLPWLVNSTDGDN  
       VLLTLDVSEEQDFSFLLYLRPVPDALKSLWKYKNLTGPQNITLNTDLVPCLCIQVWSLEPDSERVEFCPFRE  
       DPGAHRNLWHIARLRVLSPGVWQLDAPCCLPQKVTLCWQAPDQSPCQPLVPPVPQKNATVNEPQDFQLVAGH  
       PNLCVQVSTWEKVQLQACLWADSLGPFKDDMLLVEMKTGLNNTSVCALEPSGCTPLPSMASTRAARLGEELL  
       QDFRSHQCMQLWNDDNMGSLWACPMCKYIHRRWVVLVWLACLLLAALFFFLLLKKDRRKAARGSRATALLHS  
       ADGAGYERLVGALASALSQMPLRVAVDLWSRRELSAHGALAWFHHQRRRILQEGGVILLFSPAAVAQCQW  
       LQLQTVPEPGPHDALAAWLSVLPDFLQGRATGRYVGVIYFDGLLHPDSVPSPFVRVAPLFLSLPSQLPAFLDALQ  
       GGCSTSAGRPADRVERVTQALRSALDSCTSSSEAPGCCEEWDLGPCTTLE.

25

Reverse translation of rodent, e.g., mouse, DCRS7 (SEQ ID NO: 12):

atgccngtnw sntgggttyt nytnwsnytn gcnytnngnm gnaayccngt ngtnngtnwsn 60

30      ytnngarmgny tnatggarcc ncargayacn gcnmgntgyw snytnnggnyt nwsntgy cay 120

ytntgggag y gngaygtnyt ntgyytnccn ggnwsnytn arwsngcnc nggncngtn 180

35      ytnngtnccna cnmgnytnca racngarytn gtntnmgnt gyccncaraa racngaytgy 240

gcnytnngy tnmngntngt ngtncaaytn gcngtncaay gncaytgggc ngarccngar 300

40      gargcnggna arwsngayws ngarytnca garwsnmgna aygcnwsnyt ncargcncar 360

gtngtnytnw snttycargc ntayccnath gcnmgntgy cnytnytnga rgtncargtn 420

ccngcngayy tngtncarcc nggncarwsn gtnggnwsng cngtnntyga ytgytgygar 480

45      gcnwsnytn gngcngargt ncarathtgg wsntayacna arccnmngta ycaraargar 540

ytnaayytna cncarcaryt nccngaytgy mgnggnytn argtnmgnga ywsnathcar 600

50      wsntgytggg tnytnccntg gytnaaytn wsnacngay gngayaaygt nytnytnacn 660

ytnngaytnw sngargarca rgayttywsn tyytntnytn ayytnmgnc ngtnccngay 720

gcnytnaarw snytnnggta yaaraaytn acnggncnc araayathac nytnaaycay 780

55      acngayytn tncntgyt ntgyathcar gtntggwsny tngarccnga ywsngarmgn 840

gtngarttyt gyccnttymg ngargayccn ggngcncaym gnaayytn gcyathgcn 900

mgnytnmgng tnytnwsncc nggngntng carytngay cncntgyt yytnccnggn 960

aargtnacny tntgytggca rgcnccngay carwsnccnt gycarccnyt ngtnccnccn 1020  
 gtnccncara araaygcnac ngtnaaygar ccncargayt tycarytngt ngcnggncay 1080  
 5 ccnaayytnt gygtncargt nwsnacntgg garaargtnc arytncargc ntgyytntgg 1140  
 gcngaywsny tnggncntt yaargaygay atgytntyng tngaratgaa racnggnytn 1200  
 10 aayaayacnw sngtntgygc nytngarccn wsnggntgya cncnytncc nwsnatggcn 1260  
 wsnacnmng cngcnmngyt ngngargar ytntyncarg ayttymgnws ncaycartgy 1320  
 atgcarytnt ggaaygayga yaayatgggn wsnytnctgg cntgyccnat ggayaartay 1380  
 15 athcaymgnm gntgggtnyt ngtnctgytn gcntgyytny tnytnccngc ngcnytncty 1440  
 ttyttyytny tnytnaaraa rgaymgnmgn aargcngcnm gnggnwsnmg nacngcnytn 1500  
 20 ytnytncayw sngcngaygg ngcnggntay garmgnytn tnggngcnytn ngcnwsngcn 1560  
 ytnwsncara tgccnytnmg ngtnccngtn gayytnctggw snmgnmngna rytwnsngcn 1620  
 cayggngcny tngcntggtt ycaycaycar mgnmgnmnga thytncarga rggnggngtn 1680  
 25 gtnathytny tnttywsncc ngcngcngtn gncartgyt arcartggyt ncarytnca 1740  
 acngtnarcc cnggncnca ygaygcnytn gncngctggy tnwsntgygt nytnccngay 1800  
 30 ttyytnca 30 gnmngcncac nggnmngntay gtngngntnt aytygaygg nytnytnca 1860  
 ccngaywsng tncnwsncc nttymgngtn gncncnytn tywsnytncc nwsncarytn 1920  
 ccngcnttyy tngaygcnytn ncargngngn tgywsnacnw sngcnggnmg nccngcngay 1980  
 35 mgngtnarm gngtnacna rgcnymngn wsngcnytn aywsntgyac nwsnwsnwn 2040  
 gargcncng gntgytgyga rgartgggay ytnggncnt gyacnacnytn ngar 2094

40 Table 3: Nucleotide and polypeptide sequences of DNAX Cytokine Receptor Subunit like  
 embodiments (DCRS8). Primate, e.g., human, embodiment (see SEQ ID NO: 13 and 14).  
 Predicted signal sequence indicated, but may vary by a few positions and depending upon cell  
 type.

45 cccacgcntc cgggccagca gcgggcggcc ggggcgcaga gaacggcctg gctgggcgag 60  
 cgcacggcc atg gcc ccg tgg ctg cag ctc tgc tcc gtc ttc ttt acg gtc 111  
 50 Met Ala Pro Trp Leu Gln Leu Cys Ser Val Phe Phe Thr Val  
 -15 -10 -5  
 aac gcc tgc ctc aac ggc tcg cag ctg gct gtn gcc gct ggc ggg tcc 159  
 Asn Ala Cys Leu Asn Gly Ser Gln Leu Ala Xaa Ala Ala Gly Gly Ser  
 -1 1 5 10  
 55 ggc cgc gcg cng gcc gcc gac acc tgt agc tgg ang gga gtg ggg cca 207  
 Gly Arg Ala Xaa Gly Ala Asp Thr Cys Ser Trp Xaa Gly Val Gly Pro  
 15 20 25 30

5	gcc agc aga aac agt ggg ctg tac aac atc acc ttc aaa tat gac aat	255
	Ala Ser Arg Asn Ser Gly Leu Tyr Asn Ile Thr Phe Lys Tyr Asp Asn	
	35 40 45	
10	tgt acc acc tac ttg aat cca gtg ggg aag cat gtg att gct gac gcc	303
	Cys Thr Thr Tyr Leu Asn Pro Val Gly Lys His Val Ile Ala Asp Ala	
	50 55 60	
15	cag aat atc acc atc agc cag tat gct tgc cat gac caa gtg gca gtc	351
	Gln Asn Ile Thr Ile Ser Gln Tyr Ala Cys His Asp Gln Val Ala Val	
	65 70 75	
20	acc att ctt tgg tcc cca ggg gcc ctc ggc atc gaa ttc ctg aaa gga	399
	Thr Ile Leu Trp Ser Pro Gly Ala Leu Gly Ile Glu Phe Leu Lys Gly	
	80 85 90	
25	ttt cgg gta ata ctg gag gag ctg aag tcg gag gga aga cag ngc caa	447
	Phe Arg Val Ile Leu Glu Leu Lys Ser Glu Gly Arg Gln Xaa Gln	
	95 100 105 110	
30	caa ctg att cta aag gat ccg aag cag ntc aac agt agc ttc aaa aga	495
	Gln Leu Ile Leu Lys Asp Pro Lys Gln Xaa Asn Ser Ser Phe Lys Arg	
	115 120 125	
35	act gga atg gaa tct caa cct ttn ctg aat atg aaa ttt gaa acg gat	543
	Thr Gly Met Glu Ser Gln Pro Xaa Leu Asn Met Lys Phe Glu Thr Asp	
	130 135 140	
40	tat ttc gta agg ttg tcc ttt tcc ttc att aaa aac gaa agc aat tac	591
	Tyr Phe Val Arg Leu Ser Phe Ser Phe Ile Lys Asn Glu Ser Asn Tyr	
	145 150 155	
45	cac cct ttc ttc ttt aga acc cga gcc tgt gac ctg ttg tta cag ccg	639
	His Pro Phe Phe Phe Arg Thr Arg Ala Cys Asp Leu Leu Leu Gln Pro	
	160 165 170	
50	gac aat cta gct tgt aaa ccc ttc tgg aag cct cgg aac ctg aac atc	687
	Asp Asn Leu Ala Cys Lys Pro Phe Trp Lys Pro Arg Asn Leu Asn Ile	
	175 180 185 190	
55	agc cag cat ggc tcg gac atg cag gtg tcc ttc gac cac gca ccg cac	735
	Ser Gln His Gly Ser Asp Met Gln Val Ser Phe Asp His Ala Pro His	
	195 200 205	
60	aac ttc ggc ttc cgt ttc ttc tat ctt cac tac aag ctc aag cac gaa	783
	Asn Phe Gly Phe Arg Phe Phe Tyr Leu His Tyr Lys Leu Lys His Glu	
	210 215 220	
65	gga cct ttc aag cga aag acc tgt aag cag gag caa act aca gag atg	831
	Gly Pro Phe Lys Arg Lys Thr Cys Lys Gln Glu Gln Thr Thr Glu Met	
	225 230 235	
70	acc agc tgc ctc ctt caa aat gtt tct cca ggg gat tat ata att gag	879
	Thr Ser Cys Leu Leu Gln Asn Val Ser Pro Gly Asp Tyr Ile Ile Glu	
	240 245 250	

	ctg	gtg	gat	gac	act	aac	aca	aca	aga	aaa	gtg	atg	cat	tat	gcc	tta	927
	Leu	Val	Asp	Asp	Thr	Asn	Thr	Thr	Arg	Lys	Val	Met	His	Tyr	Ala	Leu	
	255					260					265					270	
5	aag	cca	gtg	cac	tcc	ccg	tgg	gcc	ggg	ccc	atc	aga	gcc	gtg	gcc	atc	975
	Lys	Pro	Val	His	Ser	Pro	Trp	Ala	Gly	Pro	Ile	Arg	Ala	Val	Ala	Ile	
					275					280						285	
10	aca	gtg	cca	ctg	gta	gtc	ata	tcg	gca	ttc	gcg	acg	ctc	ttc	act	gtg	1023
	Thr	Val	Pro	Leu	Val	Val	Ile	Ser	Ala	Phe	Ala	Thr	Leu	Phe	Thr	Val	
				290					295					300			
15	atg	tgc	cgc	aag	aag	caa	caa	gaa	aat	ata	tat	tca	cat	tta	gat	gaa	1071
	Met	Cys	Arg	Lys	Lys	Gln	Gln	Glu	Asn	Ile	Tyr	Ser	His	Leu	Asp	Glu	
			305					310					315				
20	gag	agc	tct	gag	tct	tcc	aca	tac	act	gca	gca	ctc	cca	aga	gag	agg	1119
	Glu	Ser	Ser	Glu	Ser	Ser	Thr	Tyr	Thr	Ala	Ala	Leu	Pro	Arg	Glu	Arg	
		320					325					330					
	ctc	cgg	ccg	cgg	ccg	aag	gtc	ttt	ctc	tgc	tat	tcc	agt	aaa	gat	ggc	1167
	Leu	Arg	Pro	Arg	Pro	Lys	Val	Phe	Leu	Cys	Tyr	Ser	Ser	Lys	Asp	Gly	
	335					340				345						350	
25	cag	aat	cac	atg	aat	gtc	gtc	cag	tgt	ttc	gcc	tac	ttc	ctc	cag	gac	1215
	Gln	Asn	His	Met	Asn	Val	Val	Gln	Cys	Phe	Ala	Tyr	Phe	Leu	Gln	Asp	
					355					360					365		
30	ttc	tgt	ggc	tgt	gag	gtg	gct	ctg	gac	ctg	tgg	gaa	gac	ttc	agc	ctc	1263
	Phe	Cys	Gly	Cys	Glu	Val	Ala	Leu	Asp	Leu	Trp	Glu	Asp	Phe	Ser	Leu	
				370					375					380			
35	tgt	aga	gaa	ggg	cag	aga	gaa	tgg	gtc	atc	cag	aag	atc	cac	gag	tcc	1311
	Cys	Arg	Glu	Gly	Gln	Arg	Glu	Trp	Val	Ile	Gln	Lys	Ile	His	Glu	Ser	
			385					390					395				
40	cag	ttc	atc	att	gtg	gtt	tgt	tcc	aaa	ggg	atg	aag	tac	ttt	gtg	gac	1359
	Gln	Phe	Ile	Ile	Val	Val	Cys	Ser	Lys	Gly	Met	Lys	Tyr	Phe	Val	Asp	
		400					405					410					
	aag	aag	aac	tac	aaa	cac	aaa	gga	ggg	ggc	cga	ggc	tcg	ggg	aaa	gga	1407
	Lys	Lys	Asn	Tyr	Lys	His	Lys	Gly	Gly	Gly	Arg	Gly	Ser	Gly	Lys	Gly	
	415					420					425					430	
45	gag	ctc	ttc	ctg	gtg	gcg	gtg	tca	gcc	att	gcc	gaa	aag	ctc	cgc	cag	1455
	Glu	Leu	Phe	Leu	Val	Ala	Val	Ser	Ala	Ile	Ala	Glu	Lys	Leu	Arg	Gln	
					435				440						445		
50	gcc	aag	cag	agt	tcg	tcc	gcg	gcg	ctc	agc	aag	ttt	atc	gcc	gtc	tac	1503
	Ala	Lys	Gln	Ser	Ser	Ser	Ala	Ala	Leu	Ser	Lys	Phe	Ile	Ala	Val	Tyr	
				450					455					460			
	ttt	gat	tat	tcc	tgc	gag	gga	gac	gtc	ccc	ggg	atc	cta	gac	ctg	agt	1551
	Phe	Asp	Tyr	Ser	Cys	Glu	Gly	Asp	Val	Pro	Gly	Ile	Leu	Asp	Leu	Ser	
			465					470					475				
55	acc	aag	tac	aga	ctc	atg	gac	aat	ctt	cct	cag	ctc	tgt	tcc	cac	ctg	1599
	Thr	Lys	Tyr	Arg	Leu	Met	Asp	Asn	Leu	Pro	Gln	Leu	Cys	Ser	His	Leu	
		480					485					490					

	cac tcc cga gac cac ggc ctc cag gag ccg ggg cag cac acg cga cag	1647
	His Ser Arg Asp His Gly Leu Gln Glu Pro Gly Gln His Thr Arg Gln	
	495 500 505 510	
5	ggc agc aga agg aac tac ttc cgg agc aag tca ggc cgg tcc cta tac	1695
	Gly Ser Arg Arg Asn Tyr Phe Arg Ser Lys Ser Gly Arg Ser Leu Tyr	
	515 520 525	
10	gtc gcc att tgc aac atg cac cag ttt att gac gag gag ccc gac tgg	1743
	Val Ala Ile Cys Asn Met His Gln Phe Ile Asp Glu Glu Pro Asp Trp	
	530 535 540	
15	ttc gaa aag cag ttc gtt ccc ttc cat cct cct cca ctg cgc tac cgg	1791
	Phe Glu Lys Gln Phe Val Pro Phe His Pro Pro Pro Leu Arg Tyr Arg	
	545 550 555	
20	gag cca gtc ttg gag aaa ttt gat tgc ggc ttg gtt tta aat gat gtc	1839
	Glu Pro Val Leu Glu Lys Phe Asp Ser Gly Leu Val Leu Asn Asp Val	
	560 565 570	
	atg tgc aaa cca ggg cct gag agt gac ttc tgc cta aag gta gag gcg	1887
	Met Cys Lys Pro Gly Pro Glu Ser Asp Phe Cys Leu Lys Val Glu Ala	
	575 580 585 590	
25	gct gtt ctt ggg gca acc gga cca gcc gac tcc cag cac gag agt cag	1935
	Ala Val Leu Gly Ala Thr Gly Pro Ala Asp Ser Gln His Glu Ser Gln	
	595 600 605	
30	cat ggg ggc ctg gac caa gac ggg gag gcc cgg cct gcc ctt gac ggt	1983
	His Gly Gly Leu Asp Gln Asp Gly Glu Ala Arg Pro Ala Leu Asp Gly	
	610 615 620	
35	agc gcc gcc ctg caa ccc ctg ctg cac acg gtg aaa gcc ggc agc ccc	2031
	Ser Ala Ala Leu Gln Pro Leu Leu His Thr Val Lys Ala Gly Ser Pro	
	625 630 635	
40	tcg gac atg ccg cgg gac tca ggc atc tat gac tcg tct gtg ccc tca	2079
	Ser Asp Met Pro Arg Asp Ser Gly Ile Tyr Asp Ser Ser Val Pro Ser	
	640 645 650	
	tcc gag ctg tct ctg cca ctg atg gaa gga ctc tcg acg gac cag aca	2127
	Ser Glu Leu Ser Leu Pro Leu Met Glu Gly Leu Ser Thr Asp Gln Thr	
	655 660 665 670	
45	gaa acg tct tcc ctg acg gag agc gtg tcc tcc tct tca ggc ctg ggt	2175
	Glu Thr Ser Ser Leu Thr Glu Ser Val Ser Ser Ser Ser Gly Leu Gly	
	675 680 685	
50	gag gag gaa cct cct gcc ctt cct tcc aag ctc ctc tct tct ggg tca	2223
	Glu Glu Glu Pro Pro Ala Leu Pro Ser Lys Leu Leu Ser Ser Gly Ser	
	690 695 700	
55	tgc aaa gca gat ctt ggt tgc cgc agc tac act gat gaa ctc cac gcg	2271
	Cys Lys Ala Asp Leu Gly Cys Arg Ser Tyr Thr Asp Glu Leu His Ala	
	705 710 715	
	gtc gcc cct ttg taacaaaacg aaagagtcta agcattgccca ctttagctgc	2323
	Val Ala Pro Leu	
	720	

5 tgccctccctc tgattcccca gctcatctcc ctggttgcat ggcccacttg gagctgaggt 2383  
 ctcatacaag gatatttgga gtgaaatgct ggccagtact tgttctccct tgccccaacc 2443  
 ctttaccgga tatcttgaca aactctccaa ttttctaaaa tgatatggag ctctgaaagg 2503  
 catgtccata aggtctgaca acagcttgcc aaatttggtt agtccttgga tcagagcctg 2563  
 10 ttgtgggagg tagggaggaa atatgtaaag aaaaacagga agatacctgc actaatcatt 2623  
 cagacttcat tgagctctgc aaactttgcc tgtttgctat tggctacctt gatttgaaat 2683  
 gctttgtgaa aaaaggcact tttaacatca tagccacaga aatcaagtgc cagtctatct 2743  
 15 ggaatccatg ttgtattgca gataatgttc tcatttattt ttg 2786

20 MAPWLQLCSVFFTVNACLNGSQLAVAAGGSGRAXGADTCSWXGVGPASRNSGLYNITFKYDNCCTTYLNPVGK  
 HVIADAQNITISQYACHDQVAVTILWSPGALGIEFLKGFVRVILEELKSEGRQXQQLILKDPKQXNSSFKRTG  
 MESQPXLNMKFETDYFVRLSFSFIKNESNYHPFFFRTRACDLLLPDNLACKPFWKPRNLNISQHGSDMQVS  
 FDHAPHNFGFRFFYLHYKLKHEGPFKRKTKQEQTTTSCLLQNVSPGDYIIELVDDTNTTRKVMHYALKP  
 VHSPWAGPIRAVAITVPLVVISAFATLFTVMCRKKQENIYSHLDEESSESSTYTAALPRERLRPRPKVFLC  
 YSSKDGQNHMNVVQCFAYFLQDFCGCEVALDLWEDFSLCREGQREWVIQKIHESQFIIIVVCSKGMKYFVDKK  
 25 NYKHKGGRGSGKGELFLVAVSAIAEKLKQAKQSSAALSFKFIQVYFDYSCGDVPGILDSTKYRLMDNLP  
 QLCSHLHSDHGLQEPGQHTROGSRNRYFRSKSGRSLYAICNMHQFIDEEDWFEKQFVFPFHPPLRYREP  
 VLEKFDGLVNDVMCKPGPESDFCLKVEAAVLGATGPADSQHSQHGGLDQDGEARPALDGSAAALQPLLHT  
 VKAGSPSDMPRDSGIYDSSVPSELPLMEGLSTDQTETSSLTESVSSSSGLGEEEPALPSKLLSSGSK  
 ADLGCRSYTDELHAVAPL.

30 Reverse translation of primate, e.g., human, DCRS8 (SEQ ID NO: 15):

atggcnccnt ggytnccaryt ntgywsngtn ttyttyacng tnaaygcntg yytnaayggn 60  
 35 wsncarytng cngtngcngc nggnggnwns ggnmgngcnn nngngngnga yacntgywsn 120  
 tggnnngngng tnggncngc nwsnmgnaay wsnggnytn tnaayathac nttyaartay 180  
 40 gayaaytgga cnacntayyt naaycngtn ggnaarcayg tnathgnga ygcncaraay 240  
 athacnathw sncartaygc ntgycaygay cargtngcng tnacnathyt ntggwsnccn 300  
 ggngcnytn gnatthgartt yytnaarggn ttmngngtna thytnngarga rytnaarwsn 360  
 45 gargngmgnc arnnncarca rytnathytn aargayccna arcarnnnaa ywsnwsntty 420  
 aarmgnaeng gnatggarws ncarccnnnn ytnaayatga arttygarac ngaytaytty 480  
 50 gtnmgnytnw snttywsntt yathaaraay garwsnaayt aycayccntt yttyttymgn 540  
 acnmngngent gygayytnyt nytnccarccn gayaayytng cntgyaarcc nttytggaar 600  
 ccnmgnaayy tnaayathws ncarcayggn wsngayatgc argtnwsntt ygaycaygcn 660  
 55 ccncayaayt tyggnttymg nttyttytay ytncaytaya arytnaarca ygargngcnn 720  
 ttyaarmgna aracntgyaa rcargarcar acnacngara tgacnwsntg yytnytnar 780  
 aaygtnwsnc cngngayta yathathgar ytnngngayg ayacnaayac nacnmgnaar 840

gtnatgcayt aygcnytnaa rccngtncay wsnccntggg cnggnccnat hmgngcngtn 900  
 5 gcnathacng tncnytngt ngtnathwsn gcnttygcna cnytnntyac ngtnatgtgy 960  
 mgnaraarc arcargaraa yathtaywsn cayytngayg argarwsnws ngarwsnwsn 1020  
 acntayacng cngcnytncc nmngngarmgn ytnmgncnm gncnaargt nttyyntgy 1080  
 10 taywsnwsna argayggna raaycayatg aaygtngtnc artgyttygc ntayttyytn 1140  
 cargayttyt gygntgyga rgtngcnytn gayytnagg argayttyw nyntgymgn 1200  
 15 gargncarm gngartgggt nathcaraar athcaygarw sncarttyat hathgtngtn 1260  
 tgywsnaarg gnatgaarta yttygtngay aaraaraayt ayaarcayaa rggngnggn 1320  
 mgnggnwsng gnaargnga rytnttyytn gtngcngtnw sngcnathgc ngaraarytn 1380  
 20 mgncargcna arcarwsnws nwsngcngcn ytnwsnaart tyathgcngt ntayttygay 1440  
 taywsntgyg arggngaygt nccnggnath ytngayytnw snacnaarta ymgnytatg 1500  
 25 gayaayytn cncarytngt ywsncayytn caywsnmngn aycayggyt ncargarccn 1560  
 ggnarcaya cnmgncargg nwsnmgnmgn aaytaytym gnwsnaarws nggnmgnwsn 1620  
 ytnaygtng cnathtgyaa yatgcaycar ttyathgayg argarccnga ytggttygar 1680  
 30 aarcarttyg tncnttyca yccnccnccn ytnmgntaym gngarccngt nytngaraar 1740  
 ttygaywsng gnytngtnyt naaygaygt atgtgyaarc cngnccnga rwsngaytty 1800  
 35 tgyytnaarg tngargcngc ngtnytnngn gcnaaggnc cngcngayws ncarcaygar 1860  
 wsnarcayg gnggnytna ycargaygn gargcnmgnc cngcnytna yggnwsngcn 1920  
 gcnynarc cnytnytnca yacngtnaar gcnggnwsnc cnwsngayat gccnmngay 1980  
 40 wsggnatht aygaywsnws ngtnccnwsn wsgarytnw snytnccnyt natggarggn 2040  
 ytnwsnacng aycaracnga racnwsnwsn ytnacngarw sngtnwsnws nwsnwsngn 2100  
 45 ytnngngarg argarccncc ngcnytnccn wsnaarytny tnwsnwsngg nwsntgyaar 2160  
 gcngayytn gntgymgnws ntayacngay garytncayg cngtngcncc nytn 2214

50 Table 4: Nucleotide and polypeptide sequences of DNAX Cytokine Receptor Subunit like  
 embodiments (DCRS9). Primate, e.g., human, embodiment (see SEQ ID NO: 16 and 17).  
 Predicted signal sequence indicated, but may vary by a few positions and depending upon cell  
 type.

55 atg ggg agc tcc aga ctg gca gcc ctg ctc ctg cct ctc ctc ctc ata 48  
 Met Gly Ser Arg Leu Ala Ala Leu Leu Leu Pro Leu Leu Leu Ile  
 -20 -15 -10

	gtc atc gac ctc tct gac tct gct ggg att ggc ttt cgc cac ctg ccc	96
	Val Ile Asp Leu Ser Asp Ser Ala Gly Ile Gly Phe Arg His Leu Pro	
	-5 -1 1 5	
5	cac tgg aac acc cgc tgt cct ctg gcc tcc cac acg gaa gtt ctg cct	144
	His Trp Asn Thr Arg Cys Pro Leu Ala Ser His Thr Glu Val Leu Pro	
	10 15 20 25	
10	ata tcc ctt gcc gca cct ggt ggg ccc tct tct cca caa agc ctt ggt	192
	Ile Ser Leu Ala Ala Pro Gly Gly Pro Ser Ser Pro Gln Ser Leu Gly	
	30 35 40	
15	gtg tgc gag tct ggc act gtt ccc gct gtt tgt gcc agc atc tgc tgt	240
	Val Cys Glu Ser Gly Thr Val Pro Ala Val Cys Ala Ser Ile Cys Cys	
	45 50 55	
20	cag gtg gct cag gtc ttc aac ggg gcc tct tcc acc tcc tgg tgc aga	288
	Gln Val Ala Gln Val Phe Asn Gly Ala Ser Ser Thr Ser Trp Cys Arg	
	60 65 70	
25	aat cca aaa agt ctt cca cat tca agt tct ata gga gac aca aga tgc	336
	Asn Pro Lys Ser Leu Pro His Ser Ser Ser Ile Gly Asp Thr Arg Cys	
	75 80 85	
30	cag cac ctg ctc aga gga agc tgc tgc ctc gtc gtc acc tgt ctg aga	384
	Gln His Leu Leu Arg Gly Ser Cys Cys Leu Val Val Thr Cys Leu Arg	
	90 95 100 105	
35	aga gcc atc aca ttt cca tcc cct ccc cag aca tct ccc aca agg gac	432
	Arg Ala Ile Thr Phe Pro Ser Pro Pro Gln Thr Ser Pro Thr Arg Asp	
	110 115 120	
40	ttc gct cta aaa gga ccc aac ctt cgg atc cag aga cat ggg aaa gtc	480
	Phe Ala Leu Lys Gly Pro Asn Leu Arg Ile Gln Arg His Gly Lys Val	
	125 130 135	
45	ttc cca gat tgg act cac aaa ggc atg gag gtg ggc act ggg tac aac	528
	Phe Pro Asp Trp Thr His Lys Gly Met Glu Val Gly Thr Gly Tyr Asn	
	140 145 150	
50	agg aga tgg gtt cag ctg agt ggt gga ccc gag ttc tcc ttt gat ttg	576
	Arg Arg Trp Val Gln Leu Ser Gly Gly Pro Glu Phe Ser Phe Asp Leu	
	155 160 165	
55	ctg cct gag gcc cgg gct att cgg gtg acc ata tct tca ggc cct gag	624
	Leu Pro Glu Ala Arg Ala Ile Arg Val Thr Ile Ser Ser Gly Pro Glu	
	170 175 180 185	
60	gtc agc gtg cgt ctt tgt cac cag tgg gca ctg gag tgt gaa gag ctg	672
	Val Ser Val Arg Leu Cys His Gln Trp Ala Leu Glu Cys Glu Glu Leu	
	190 195 200	
65	agc agt ccc tat gat gtc cag aaa att gtg tct ggg ggc cac act gta	720
	Ser Ser Pro Tyr Asp Val Gln Lys Ile Val Ser Gly Gly His Thr Val	
	205 210 215	
70	gag ctg cct tat gaa ttc ctt ctg ccc tgt ctg tgc ata gag gca tcc	768
	Glu Leu Pro Tyr Glu Phe Leu Leu Pro Cys Leu Cys Ile Glu Ala Ser	
	220 225 230	



	tac ctg caa gag gac act gtg agg cgc aaa aaa tgt ccc ttc cag agc	816
	Tyr Leu Gln Glu Asp Thr Val Arg Arg Lys Lys Cys Pro Phe Gln Ser	
	235 240 245	
5	tgg cca gaa gcc tat ggc tgc gac ttc tgg aag tca gtg cac ttc act	864
	Trp Pro Glu Ala Tyr Gly Ser Asp Phe Trp Lys Ser Val His Phe Thr	
	250 255 260 265	
10	gac tac agc cag cac act cag atg gtc atg gcc ctg aca ctc cgc tgc	912
	Asp Tyr Ser Gln His Thr Gln Met Val Met Ala Leu Thr Leu Arg Cys	
	270 275 280	
15	cca ctg aag ctg gaa gct gcc ctc tgc cag agg cac gac tgg cat acc	960
	Pro Leu Lys Leu Glu Ala Ala Leu Cys Gln Arg His Asp Trp His Thr	
	285 290 295	
20	ctt tgc aaa gac ctc ccg aat gcc acg gct cga gag tca gat ggg tgg	1008
	Leu Cys Lys Asp Leu Pro Asn Ala Thr Ala Arg Glu Ser Asp Gly Trp	
	300 305 310	
25	tat gtt ttg gag aag gtg gac ctg cac ccc cag ctc tgc ttc aag gta	1056
	Tyr Val Leu Glu Lys Val Asp Leu His Pro Gln Leu Cys Phe Lys Val	
	315 320 325	
30	caa cca tgg ttc tct ttt gga aac agc agc cat gtt gaa tgc ccc cac	1104
	Gln Pro Trp Phe Ser Phe Gly Asn Ser Ser His Val Glu Cys Pro His	
	330 335 340 345	
35	cag act ggg tct ctc aca tcc tgg aat gta agc atg gat acc caa gcc	1152
	Gln Thr Gly Ser Leu Thr Ser Trp Asn Val Ser Met Asp Thr Gln Ala	
	350 355 360	
40	cag cag ctg att ctt cac ttc tcc tca aga atg cat gcc acc ttc agt	1200
	Gln Gln Leu Ile Leu His Phe Ser Ser Arg Met His Ala Thr Phe Ser	
	365 370 375	
45	gct gcc tgg agc ctc cca ggc ttg ggg cag gac act ttg gtg ccc ccc	1248
	Ala Ala Trp Ser Leu Pro Gly Leu Gly Gln Asp Thr Leu Val Pro Pro	
	380 385 390	
50	gtg tac act gtc agc cag gtg tgg cgg tca gat gtc cag ttt gcc tgg	1296
	Val Tyr Thr Val Ser Gln Val Trp Arg Ser Asp Val Gln Phe Ala Trp	
	395 400 405	
55	aag cac ctc ttg tgt cca gat gtc tct tac aga cac ctg ggg ctc ttg	1344
	Lys His Leu Leu Cys Pro Asp Val Ser Tyr Arg His Leu Gly Leu Leu	
	410 415 420 425	
50	atc ctg gca ctg ctg gcc ctc ctc acc cta ctg ggt gtt gtt ctg gcc	1392
	Ile Leu Ala Leu Leu Ala Leu Leu Thr Leu Leu Gly Val Val Leu Ala	
	430 435 440	
55	ctc acc tgc cgg cgc cca cag tca ggc ccg ggc cca gcg cgg cca gtg	1440
	Leu Thr Cys Arg Arg Pro Gln Ser Gly Pro Gly Pro Ala Arg Pro Val	
	445 450 455	

	ctc ctc ctg cac gcg gcg gac tcg gag gcg cag cgg cgc ctg gtg gga	1488
	Leu Leu Leu His Ala Ala Asp Ser Glu Ala Gln Arg Arg Leu Val Gly	
	460 465 470	
5	gcg ctg gct gaa ctg cta cgg gca gcg ctg ggc ggc ggg cgc gac gtg	1536
	Ala Leu Ala Glu Leu Leu Arg Ala Ala Leu Gly Gly Gly Arg Asp Val	
	475 480 485	
10	atc gtg gac ctg tgg gag ggg agg cac gtg gcg cgc gtg ggc ccg ctg	1584
	Ile Val Asp Leu Trp Glu Gly Arg His Val Ala Arg Val Gly Pro Leu	
	490 495 500 505	
15	ccg tgg ctc tgg gcg gcg cgg acg cgc gta gcg cgg gag cag ggc act	1632
	Pro Trp Leu Trp Ala Ala Arg Thr Arg Val Ala Arg Glu Gln Gly Thr	
	510 515 520	
20	gtg ctg ctg ctg tgg agc ggc gcc gac ctt cgc ccg gtc agc ggc ccc	1680
	Val Leu Leu Leu Trp Ser Gly Ala Asp Leu Arg Pro Val Ser Gly Pro	
	525 530 535	
25	gac ccc cgc gcc gcg ccc ctg ctc gcc ctg ctc cac gct gcc ccg cgc	1728
	Asp Pro Arg Ala Ala Pro Leu Leu Ala Leu Leu His Ala Ala Pro Arg	
	540 545 550	
30	ccg ctg ctg ctg ctc gct tac ttc agt cgc ctc tgc gcc aag ggc gac	1776
	Pro Leu Leu Leu Leu Ala Tyr Phe Ser Arg Leu Cys Ala Lys Gly Asp	
	555 560 565	
35	atc ccc ccg ccg ctg cgc gcc ctg ccg cgc tac cgc ctg ctg cgc gac	1824
	Ile Pro Pro Pro Leu Arg Ala Leu Pro Arg Tyr Arg Leu Leu Arg Asp	
	570 575 580 585	
40	ctg ccg cgt ctg ctg cgg gcg ctg gac gcg cgg cct ttc gca gag gcc	1872
	Leu Pro Arg Leu Leu Arg Ala Leu Asp Ala Arg Pro Phe Ala Glu Ala	
	590 595 600	
45	acc agc tgg ggc cgc ctt ggg gcg cgg cag cgc agg cag agc cgc cta	1920
	Thr Ser Trp Gly Arg Leu Gly Ala Arg Gln Arg Arg Gln Ser Arg Leu	
	605 610 615	
50	gag ctg tgc agc cgg ctc gaa cga gag gcc gcc cga ctt gca gac cta	1968
	Glu Leu Cys Ser Arg Leu Glu Arg Glu Ala Ala Arg Leu Ala Asp Leu	
	620 625 630	
55	ggt tgagcagagc tccaccgcag tcccgggtgt ctgcggccgc t	2012
	Gly	
	MGSSRLAALLPLLLIVIDLSDSAGIGFRHLPHWNTRCPLASHTEVLPISLAAPGGPSSPQSLGVCESGTVP	
	AVCASICCCQVAQVFNGASSTSWCRNPKSLPHSSSIGDTRCQHLLRGSCCLVVTCLRRATTFSPSPQTSPTRD	
	FALKGPNLRIQRHGKVFDPDWTHTKGMVEVGTGYNRRWVQLSGGPEFSFDLLPEARAIRVTISSGPEVSVRLCHQ	
	WALECEELSSPYDVQKIVSGGHTVELPYEFLLPCLCIEASYLQEDTVRRKKCPFQSWPEAYGSDFWKSVHFT	
	DYSQHTQMVMALTLRCPLKLEAALCQRHDWHTLCKDLPNATARES DGWYVLEKVDLHPQLCFKVQPFWSFGN	
	SSHVECPHQTGSLTSWNVSMDTQAQQLILHFSSRMHATFSAAWSLPGLGQDTLVPPVYTVSQVWRSDVQFAW	
	KHLLCPDVSYRHLGLLILALLALLTLLGVVLALTCCRPGSGPGPARPVLLLHAADSEAQRRLVGALAEELLRA	
	ALGGGRDVIVDLWEGRHVARVGPLPWLWAARTRVAREQGTVLLLLWSGADLRPVSGPDPRAAPLLALLHAAPR	
	PLLLLAYFSRLCAKGDIPPLRLALPRYRLRLDLPRLLRALDARPF AEATSWGRLGARQRRQSRLELCSRLE	
	EAARLADLG.	

Reverse translation of primate, e.g., human, DCRS9 (SEQ ID NO: 18):

5 atgggnwsnw snmgnytnge ngenytnytn ytncnytny tnytnathgt nathgayytn 60  
 wsn gaywsng cnggnathgg nttymgn cay ytncncayt ggaayacnmg ntgyccnytn 120  
 gcwnsn cay cngargtnyt nccnathwsn ytn gcngcnc cnggnggncc nwsnwsnccn 180  
 10 carwsnytn gngtntgyga rwsnggnacn gtncngcng tntgygc nws nathtgytgy 240  
 cargtn gcnc argtnttyaa yggngcnwsn wsnacnwsnt ggtgymgnaa yccnaarwsn 300  
 ytncncayw snwsnwsnat hggngayacn mgntgy carc ayytnytnmg nggnwsntgy 360  
 15 tgyytn gtn tncntgyt nmgnmgncn athacnttyc cnwsnccncc ncaracnwsn 420  
 ccnacnmng aytytgcn yt naarggnccn ayytnmgna thcarmgnca yggnaargtn 480  
 20 ttyccngayt ggacncayaa rggnatggar gtnggnacng gntayaaymg nmgtgggtn 540  
 carytnwsng gnggnccnga rttywsntty gayytnytn cngargcnmg ngcnathmgn 600  
 gtnacnathw snwsnggncc ngargtnwsn gtnmgnytn gycaycartg ggcnytn gar 660  
 25 tgygargary tnwsnwsncc ntaygaygn caraarathg tnwsnggngg ncayacngtn 720  
 garytnccnt aygarttyt nytnccntgy ytntgyathg argcnwsnta yytnccarg 780  
 30 gayacngtnm gnmgnaaraa rtgyccntty carwsntggc cngargcnta ygg nwsngay 840  
 ttytggaarw sngtn caytt yacngaytay wsn carcaya cncaratggt natggcn ytn 900  
 acnytnmgnt gyccnytnaa rytngargcn gcnytn tgyc armgn cayga ytggcayacn 960  
 35 ytntgyaarg ayytnccnaa ygcnacngcn mgngarwsng ayggntggta ygtnytn gar 1020  
 aargtn gayy tncayccnca rytntgytty aargtn carc cntgggtyws nttyggnaay 1080  
 40 wsnwsncayg tngartgycc ncaycaracn ggnwsnytna cnwsntggaa ygt nwsnatg 1140  
 gayacncarg cncarcaryt nathytn cay ttywsnwsnm gnatgcaygc nacnttywsn 1200  
 gcngcntggw snytnccngg nytnngncar gayacnytn tncncncgt ntayacngtn 1260  
 45 wsn cargtn gmg nwsnga ygtncartty gcntggaarc ayytnytn tgyccngaygn 1320  
 wsntaymgnc ayytnggny nytnathytn gcnytnytn cnytnytnac nytnytn ggn 1380  
 50 gtn gtnytn cnytnacntg ymgnmgnccn carwsnggnc cnggncngc nmgnccngtn 1440  
 ytnytnytn aygcngcnga ywsngargcn carmgnmgny tngtnngngc nytnngcgar 1500  
 ytnytnmgng cngcnytn gg nggnggnmgn gaygt nathg tngayytn tggarggnmgn 1560  
 55 caygtngcnm gngtnngncc nytnccntgg ytntgggng cnmg nacnmg ngtnngcnmgn 1620  
 garcarggna cngtnytn nytn tggwsn ggngcngayy tnmgnccngt nwsnggnccn 1680

	gayccnmgn g cngcncny t nytngcnytn ytnca ygcng cnccnmgnc c nytnytnytn	1740
	ytn gcntay t tywsnmgn y ntgygcnaar ggngayath c cncncncny t nmgn gcn ytn	1800
5	ccnm gntay m gnytnytnmg ngayytncn mgn ytnytnm gngcn ytn ga ygcnmgnccn	1860
	ttygcngarg cnacwsntg gggnmgn ytn ggngcnmgnc armgnmgnc a rwsnmgn ytn	1920
10	garytn tgyw snmgnytn ga rmgn gargcn gcnmgnytn g cngayytngg n	1971

Rodent, e.g., mouse, embodiment (see SEQ ID NO: 19 and 20). Predicted signal sequence indicated, but may vary by a few positions and depending upon cell type.

15	cagctccggg	ccaggccctg	ctgcctctct	gcagacagga	aagacatggt	ctctgcgccc	60
	tgatcctaca	gaagctc	atg ggg agc ccc aga ctg gca gcc ttg ctc ctg	110			
			Met Gly Ser Pro Arg Leu Ala Ala Leu Leu Leu				
			-20	-15			
20	tct ctc ccg cta ctg ctc atc ggc ctc gct gtg tct gct cgg gtt gcc	158					
	Ser Leu Pro Leu Leu Leu Ile Gly Leu Ala Val Ser Ala Arg Val Ala						
		-10	-5	-1	1		
25	tgc ccc tgc ctg cgg agt tgg acc agc cac tgt ctc ctg gcc tac cgt	206					
	Cys Pro Cys Leu Arg Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg						
	5	10	15	20			
30	gtg gat aaa cgt ttt gct ggc ctt cag tgg ggc tgg ttc cct ctc ttg	254					
	Val Asp Lys Arg Phe Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu						
		25	30	35			
	gtg agg aaa tct aaa agt cct cct aaa ttt gaa gac tat tgg agg cac	302					
	Val Arg Lys Ser Lys Ser Pro Pro Lys Phe Glu Asp Tyr Trp Arg His						
35		40	45	50			
	agg aca cca gca tcc ttc cag agg aag ctg cta ggc agc cct tcc ctg	350					
	Arg Thr Pro Ala Ser Phe Gln Arg Lys Leu Leu Gly Ser Pro Ser Leu						
		55	60	65			
40	tct gag gaa agc cat cga att tcc atc ccc tcc tca gcc atc tcc cac	398					
	Ser Glu Glu Ser His Arg Ile Ser Ile Pro Ser Ser Ala Ile Ser His						
	70	75	80				
45	aga ggc caa cgc acc aaa agg gcc cag cct tca gct gca gaa gga aga	446					
	Arg Gly Gln Arg Thr Lys Arg Ala Gln Pro Ser Ala Ala Glu Gly Arg						
	85	90	95	100			
50	gaa cat ctc cct gaa gca ggg tca caa aag tgt gga gga cct gaa ttc	494					
	Glu His Leu Pro Glu Ala Gly Ser Gln Lys Cys Gly Gly Pro Glu Phe						
		105	110	115			
	tcc ttt gat ttg ctg ccc gag gtg cag gct gtt cgg gtg act att cct	542					
	Ser Phe Asp Leu Leu Pro Glu Val Gln Ala Val Arg Val Thr Ile Pro						
55		120	125	130			

	gca ggc ccc aag gca cgt gtg cgc ctt tgt tat cag tgg gca ctg gaa	590
	Ala Gly Pro Lys Ala Arg Val Arg Leu Cys Tyr Gln Trp Ala Leu Glu	
	135 140 145	
5	tgt gaa gac ttg agt agc cct ttt gat acc cag aaa att gtg tct gga	638
	Cys Glu Asp Leu Ser Ser Pro Phe Asp Thr Gln Lys Ile Val Ser Gly	
	150 155 160	
10	ggg cac act gta gac ctg cct tat gaa ttc ctt ctg ccc tgc atg tgc	686
	Gly His Thr Val Asp Leu Pro Tyr Glu Phe Leu Leu Pro Cys Met Cys	
	165 170 175 180	
15	ata gag gcc tcc tac ctg caa gag gac act gtg agg cgc aaa agt gtc	734
	Ile Glu Ala Ser Tyr Leu Gln Glu Asp Thr Val Arg Arg Lys Ser Val	
	185 190 195	
20	cct tcc aga gct ggc ctg aag ctt atg gct cag act tct ggc agt caa	782
	Pro Ser Arg Ala Gly Leu Lys Leu Met Ala Gln Thr Ser Gly Ser Gln	
	200 205 210	
25	tac gct tca ctg act aca gcc agc ac	808
	Tyr Ala Ser Leu Thr Thr Ala Ser	
	215 220	
30	Reverse translation of rodent, e.g., mouse, DCRS9 (SEQ ID NO: 21):	
	atgggnwsnc cnmgnytngc ngcnytnytn ytnwsnytn cnytnytnytn nathggnytn	60
35	gcngtnwsng cnmgngtngc ntgyccntgy ytnmgnwsnt ggacnwsnca ytgyytnytn	120
	gcntaymgng tngayaarmg nttygcnggn ytncartggg gntgggtycc nytnytnytn	180
40	mgnaarwsna arwsnccncc naarttygar gaytaytggm gncaymgnc nccngcnwsn	240
	ttycarmgna arytnytnng nwsnccnwsn ytnwsngarg arwsncaymg nathwsnath	300
	ccnwsnwsng cnathwsnca ymgnggncar mgncacnaarm gngcncarcc nwsngcngcn	360
45	garggnmgng arcayytncc ngargcnggn wncaraart gyggnggnc ngarttywsn	420
	ttygayytny tnccngargt ncargcngtn mgngtnacna thccngcngg nccnaargcn	480
50	mgngtnmgny tntgytayca rtgggcnyn gartgygarg ayytnwsnws nccnttygay	540
	acncaraara thgtnwsngg nggncayacn gtngayytn cntaygartt yytnytnccn	600
	tgyatgtgya thgargcnws ntayytn car gargayacng tnmgnmgnaa rwsngtnccn	660
55	wsnmgngcng gnytnaaryt natggcncar acnwsnggnw sncartaygc nwsnytnacn	720
	acngcnwsn	729

Table 5: Nucleotide and polypeptide sequences of DNAX Cytokine Receptor Subunit like embodiments (DCRS10). Primate, e.g., human, embodiment (see SEQ ID NO: 22 and 23).

5	ttttgagcag aggccttccta ggctccgtag aaatttgcat acagcttcca cttcctgctt	60
	cagagcctgt tcttctactt acctgggccc ggagaagggtg gagggagacg agaagccgcc	120
	gagagccgac taccctccgg gccagctctg tctgtccgtg gtggatctaa gaaactaga	179
10	atg aac cga agc att cct gtg gag gtt gat gaa tca gaa cca tac cca	227
	Met Asn Arg Ser Ile Pro Val Glu Val Asp Glu Ser Glu Pro Tyr Pro	
	1 5 10 15	
15	agt cag ttg ctg aaa cca atc cca gaa tat tcc ccg gaa gag gaa tca	275
	Ser Gln Leu Leu Lys Pro Ile Pro Glu Tyr Ser Pro Glu Glu Glu Ser	
	20 25 30	
20	gaa cca cct gct cca aat ata agg aac atg gca ccc aac agc ttg tct	323
	Glu Pro Pro Ala Pro Asn Ile Arg Asn Met Ala Pro Asn Ser Leu Ser	
	35 40 45	
25	gca ccc aca atg ctt cac aat tcc tcc gga gac ttt tct caa gct cac	371
	Ala Pro Thr Met Leu His Asn Ser Ser Gly Asp Phe Ser Gln Ala His	
	50 55 60	
30	tca acc ctg aaa ctt gca aat cac cag cgg cct gta tcc cgg cag gtc	419
	Ser Thr Leu Lys Leu Ala Asn His Gln Arg Pro Val Ser Arg Gln Val	
	65 70 75 80	
35	acc tgc ctg cgc act caa gtt ctg gag gac agt gaa gac agt ttc tgc	467
	Thr Cys Leu Arg Thr Gln Val Leu Glu Asp Ser Glu Asp Ser Phe Cys	
	85 90 95	
40	agg aga cac cca ggc ctg ggc aaa gct ttc cct tct ggg tgc tct gca	515
	Arg Arg His Pro Gly Leu Gly Lys Ala Phe Pro Ser Gly Cys Ser Ala	
	100 105 110	
45	gtc agc gag cct gcg tct gag tct gtg gtt gga gcc ctc cct gca gag	563
	Val Ser Glu Pro Ala Ser Glu Ser Val Val Gly Ala Leu Pro Ala Glu	
	115 120 125	
50	cat cag ttt tca ttt atg gaa aaa cgt aat caa tgg ctg gta tct cag	611
	His Gln Phe Ser Phe Met Glu Lys Arg Asn Gln Trp Leu Val Ser Gln	
	130 135 140	
55	ctt tca gcg gct tct cct gac act ggc cat gac tca gac aaa tca gac	659
	Leu Ser Ala Ala Ser Pro Asp Thr Gly His Asp Ser Asp Lys Ser Asp	
	145 150 155 160	
60	caa agt tta cct aat gcc tca gca gac tcc ttg ggc ggt agc cag gag	707
	Gln Ser Leu Pro Asn Ala Ser Ala Asp Ser Leu Gly Gly Ser Gln Glu	
	165 170 175	
65	atg gtg caa cgg ccc cag cct cac agg aac cga gca ggc ctg gat ctg	755
	Met Val Gln Arg Pro Gln Pro His Arg Asn Arg Ala Gly Leu Asp Leu	
	180 185 190	

	cca acc ata gac acg gga tat gat tcc cag ccc cag gat gtc ctg ggc	803
	Pro Thr Ile Asp Thr Gly Tyr Asp Ser Gln Pro Gln Asp Val Leu Gly	
	195 200 205	
5	atc agg cag ctg gaa agg ccc ctg ccc ctc acc tcc gtg tgt tac ccc	851
	Ile Arg Gln Leu Glu Arg Pro Leu Pro Leu Thr Ser Val Cys Tyr Pro	
	210 215 220	
10	cag gac ctc ccc aga cct ctc agg tcc agg gag ttc cct cag ttt gaa	899
	Gln Asp Leu Pro Arg Pro Leu Arg Ser Arg Glu Phe Pro Gln Phe Glu	
	225 230 235 240	
15	cct cag agg tat cca gca tgt gca cag atg ctg cct ccc aat ctt tcc	947
	Pro Gln Arg Tyr Pro Ala Cys Ala Gln Met Leu Pro Pro Asn Leu Ser	
	245 250 255	
20	cca cat gct cca tgg aac tat cat tac cat tgt cct gga agt ccc gat	995
	Pro His Ala Pro Trp Asn Tyr His Tyr His Cys Pro Gly Ser Pro Asp	
	260 265 270	
	cac cag gtg cca tat ggc cat gac tac cct cga gca gcc tac cag caa	1043
	His Gln Val Pro Tyr Gly His Asp Tyr Pro Arg Ala Ala Tyr Gln Gln	
	275 280 285	
25	gtg atc cag ccg gct ctg cct ggg cag ccc ctg cct gga gcc agt gtg	1091
	Val Ile Gln Pro Ala Leu Pro Gly Gln Pro Leu Pro Gly Ala Ser Val	
	290 295 300	
30	aga ggc ctg cac cct gtg cag aag gtt atc ctg aat tat ccc agc ccc	1139
	Arg Gly Leu His Pro Val Gln Lys Val Ile Leu Asn Tyr Pro Ser Pro	
	305 310 315 320	
35	tgg gac caa gaa gag agg ccc gca cag aga gac tgc tcc ttt ccg ggg	1187
	Trp Asp Gln Glu Arg Pro Ala Gln Arg Asp Cys Ser Phe Pro Gly	
	325 330 335	
40	ctt cca agg cac cag gac cag cca cat cac cag cca cct aat aga gct	1235
	Leu Pro Arg His Gln Asp Gln Pro His His Gln Pro Pro Asn Arg Ala	
	340 345 350	
	ggg gct cct ggg gag tcc ttg gag tgc cct gca gag ctg aga cca cag	1283
	Gly Ala Pro Gly Glu Ser Leu Glu Cys Pro Ala Glu Leu Arg Pro Gln	
	355 360 365	
45	gtt ccc cag cct ccg tcc cca gct gct gtg cct aga ccc cct agc aac	1331
	Val Pro Gln Pro Pro Ser Pro Ala Ala Val Pro Arg Pro Pro Ser Asn	
	370 375 380	
50	cct cca gcc aga gga act cta aaa aca agc aat ttg cca gaa gaa ttg	1379
	Pro Pro Ala Arg Gly Thr Leu Lys Thr Ser Asn Leu Pro Glu Glu Leu	
	385 390 395 400	
55	cgg aaa gtc ttt atc act tat tgc atg gac aca gct atg gag gtg gtg	1427
	Arg Lys Val Phe Ile Thr Tyr Ser Met Asp Thr Ala Met Glu Val Val	
	405 410 415	
	aaa ttc gtg aac ttt ttg ttg gta aat ggc ttc caa act gca att gac	1475
	Lys Phe Val Asn Phe Leu Leu Val Asn Gly Phe Gln Thr Ala Ile Asp	
	420 425 430	

ata ttt gag gat aga atc cga ggc att gat atc att aaa tgg atg gag 1523  
 Ile Phe Glu Asp Arg Ile Arg Gly Ile Asp Ile Ile Lys Trp Met Glu  
 435 440 445

5

cgc tac ctt agg gat aag acc gtg atg ata atc gta gca atc agc ccc 1571  
 Arg Tyr Leu Arg Asp Lys Thr Val Met Ile Ile Val Ala Ile Ser Pro  
 450 455 460

10

aaa tac aaa cag gac gtg gaa ggc gct gag tcg cag ctg gac gag gat 1619  
 Lys Tyr Lys Gln Asp Val Glu Gly Ala Glu Ser Gln Leu Asp Glu Asp  
 465 470 475 480

15

gag cat ggc tta cat act aag tac att cat cga atg atg cag att gag 1667  
 Glu His Gly Leu His Thr Lys Tyr Ile His Arg Met Met Gln Ile Glu  
 485 490 495

20

ttc ata aaa caa gga agc atg aat ttc aga ttc atc cct gtg ctc ttc 1715  
 Phe Ile Lys Gln Gly Ser Met Asn Phe Arg Phe Ile Pro Val Leu Phe  
 500 505 510

25

cca aat gct aag aag gag cat gtg ccc acc tgg ctt cag aac act cat 1763  
 Pro Asn Ala Lys Lys Glu His Val Pro Thr Trp Leu Gln Asn Thr His  
 515 520 525

30

gtc tac agc tgg ccc aag aat aaa aaa aac atc ctg ctg cgg ctg ctg 1811  
 Val Tyr Ser Trp Pro Lys Asn Lys Lys Asn Ile Leu Leu Arg Leu Leu  
 530 535 540

35

aga gag gaa gag tat gtg gct cct cca cgg ggg cct ctg ccc acc ctt 1859  
 Arg Glu Glu Glu Tyr Val Ala Pro Pro Arg Gly Pro Leu Pro Thr Leu  
 545 550 555 560

cag gtg gtt ccc ttg tgacaccgtt catccccaga tcaactgaggc caggccatgt 1914  
 Gln Val Val Pro Leu  
 565

40

ttggggcctt gttctgacag cattctggct gaggetggtc ggtagcactc ctggctgggtt 1974  
 tttttctgtt cctccccgag aggccctctg gccccagga aacctgttgt gcagagctct 2034  
 tccccggaga cctccacaca ccctggcttt gaagtggagt ctgtgactgc tctgcattct 2094  
 ctgcttttaa aaaaaccatt gcaggtgcca gtgtcccata tgttcctcct gacagtttga 2154  
 tgtgtccatt ctgggcctct cagtgccttag caagtagata atgtaagggg tgtggcagca 2214  
 aatggaaatg actacaaaca ctctcctatc aatcacttca ggctactttt atgagtttagc 2274  
 cagatgcttg tgtatcctca gaccaaaactg attcatgtac aaataataaa atgtttactc 2334  
 ttttgtaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa 2377



5 MNRSIPVEVDESEPYPSQLLKPIPEYSPREESEPPAPNIRNMAPNSLSAPTMLHNSSGDFSQAHSTLKLANH  
 QRPVSRQVTCRLRTQVLEDSFDCRRHPGLGKAFFSGCSAVSEPASESVVGALPAEHQFSFMEKRNQWLVSQ  
 LSAASPDTHGSDSDQSLPNASADSLGGSQEMVQRQPQPHNRAGLDLPTIDTGYSQPDVLRQLERPL  
 10 PLTSVCYPQDLPRPLRSREFFQFEPQRYPACAQMLPPNLSHPAPWNYHYHCPGSPDHQVPYGHDPRAAYQQ  
 VIQPALEPGQPLPGASVRGLHPVQKVILNYPSPWDQEERPAQRDCSFPGLPRHQDQPHHQPNNRAGAPGESLE  
 CPAELRPQVPQPPSPAAPVPRPPSNPPARGTLKTSNLPEELRKVFITYSMDTAMEVVKFVNFLLVNGFQTAID  
 IFEDRIRGIDIKWMEYLRDKTVMIIVAISPKYKQDVEGAESQLDEDEHGLHTKYIHRMMQIEFIKQGSMN  
 FRFIPVLFPNAKKEHVPTWLQNTHVYSWPKNKNILLRLLREEYVAPPRGPLPTLQVVPL

Reverse translation of primate, e.g., human, DCRS10 (SEQ ID NO: 24):

15 atgaaymgw snathccngt ngargtngay garwsngarc cntayccnws ncarytnytn 60  
 aarccnathc cngartayws nccngargar garwsngarc cncngcnc naayathmgn 120  
 aayatggcnc cnaaywsnyt nwsngcncn acnatgytnc ayaaywsnws ngngaytty 180  
 20 wsnarcgnc aywsnacnyt naarytngcn aaycaycarm gncngtnws nmgnarcgtn 240  
 acntgyytnm gnacncargt nytngargay wsngargayw snttytgymg nmgnayccn 300  
 ggnytnngna argcnttycc nwsngntgy wsngcngtnw sngarcncg nwsngarwsn 360  
 25 gtngtnngng cnytnccngc ngarcaycar ttywsnttya tggaraarmg naaycartgg 420  
 ytngtnwsnc arytnwsngc ngcnwsnccn gayacnggnc aygaywsnga yaarwsngay 480  
 30 carwsnytn cnaaygcnws ngcngaywsn ytngngngw sncargarat ggtncarmgn 540  
 ccncarcnc aymgnaaymg ngcngnytn gayytnccna cnathgayac nggntaygay 600  
 wsnarcnc argaygtnyt nggnathmgn carytngarm gncnytncc nytnacnwsn 660  
 35 gtntgytayc cncargayyt nccnmgnccn ytnmgnwsnm gngarttycc ncarttygar 720  
 ccncarmgnt ayccngcntg ygncaratg ytncncncna ayytnwsncc ncaygcncn 780  
 40 tggaaytayc aytaycaytg yccngnwsn ccngaycayc argtnccnta yggncaygay 840  
 tayccnmng cngcntayca rcargtnath carcngcny tncnggnca rccnytnccn 900  
 ggngcnwsng tnmnggnytn ncayccngtn caraargtna thytnaayta yccnwsnccn 960  
 45 tgggaycarg argarmgncc ngcncarmgn gaytgywsnt tyccnggnytn nccnmgnay 1020  
 cargaycarc ncaycayca rccnccnaay mgngcngng cncnggnga rwsnytngar 1080  
 50 tgyccngcng arytnmgncc ncargtnccn carcncncw snccngcngc ngtnccnmgn 1140  
 ccncnwsna ayccncngc nmngngnacn ytnaaracnw snaayytncc ngargarytn 1200  
 mgnaargtn tyathacnta ywsnatggay acngcnatgg argtngtnaa rtytgtnaay 1260  
 55 ttyytnytn tnaaygntt ycaracngcn athgayatht tygargaymg nathmnggn 1320  
 athgayatha thaartggat ggarmgntay ytnmngnaya aracngtnat gathathgtn 1380

gcnathwsnc cnaartayaa rcargaygtg garggngcng arwsncaryt ngaygargay 1440  
 garcayggny tncayacnaa rtayathcay mgnatgatgc arathgartt yathaarcay 1500  
 5 ggnwsnatga ayttymgntt yathccngtn ytnttyccna aygcnaaraa rgarcaygtg 1560  
 ccnacttggy tncaraayac ncaygtntay wsntggccna araayaaraa raayathytn 1620  
 ytnmgnytny tnmngngarga rgartaygtg gcncncncnm gnggncnnyt nccnacytn 1680  
 10 cagtngtnc cnytn 1695

Rodent, e.g., mouse, embodiment (see SEQ ID NO: 25 and 26).

15 cag gac ctc cct ggg cct ctg agg tcc agg gaa ttg cca cct cag ttt 48  
 Gln Asp Leu Pro Gly Pro Leu Arg Ser Arg Glu Leu Pro Pro Gln Phe  
 1 5 10 15

20 gaa ctt gag agg tat cca atg aac gcc cag ctg ctg ccg ccc cat cct 96  
 Glu Leu Glu Arg Tyr Pro Met Asn Ala Gln Leu Leu Pro Pro His Pro  
 20 25 30

25 tcc cca cag gcc cca tgg aac tgt cag tac tac tgc ccc gga ggg ccc 144  
 Ser Pro Gln Ala Pro Trp Asn Cys Gln Tyr Tyr Cys Pro Gly Gly Pro  
 35 40 45

30 tac cac cac cag gtg cca cac ggc cat ggc tac cct cca gca gca gcc 192  
 Tyr His His Gln Val Pro His Gly His Gly Tyr Pro Pro Ala Ala Ala  
 50 55 60

35 tac cag caa gta ctc cag cct gct ctg cct ggg cag gtc ctt cct ggg 240  
 Tyr Gln Gln Val Leu Gln Pro Ala Leu Pro Gly Gln Val Leu Pro Gly  
 65 70 75 80

gca agg gca aga ggc cca cgc cct gtg cag aag gtc atc ctg aat gac 288  
 Ala Arg Ala Arg Gly Pro Arg Pro Val Gln Lys Val Ile Leu Asn Asp  
 85 90 95

40 tcc agc ccc caa gac caa gaa gag aga cct gca cag aga gac ttc tct 336  
 Ser Ser Pro Gln Asp Gln Glu Glu Arg Pro Ala Gln Arg Asp Phe Ser  
 100 105 110

45 ttc ccg agg ctc ccg agg gac cag ctc tac cgc cca cca tct aat gga 384  
 Phe Pro Arg Leu Pro Arg Asp Gln Leu Tyr Arg Pro Pro Ser Asn Gly  
 115 120 125

50 gtg gaa gcc cct gag gag tcc ttg gac ctt cct gca gag ctg aga cca 432  
 Val Glu Ala Pro Glu Glu Ser Leu Asp Leu Pro Ala Glu Leu Arg Pro  
 130 135 140

55 cat ggt ccc cag gct cca tcc cta gct gcc gtg cct aga ccc cct agc 480  
 His Gly Pro Gln Ala Pro Ser Leu Ala Ala Val Pro Arg Pro Pro Ser  
 145 150 155 160

aac ccc tta gcc cga gga act cta aga acc agc aat ttg cca gaa gaa 528  
 Asn Pro Leu Ala Arg Gly Thr Leu Arg Thr Ser Asn Leu Pro Glu Glu  
 165 170 175

	tta cgg aaa gtc ttt atc act tat tct atg gac aca gcc atg gag gtg	576
	Leu Arg Lys Val Phe Ile Thr Tyr Ser Met Asp Thr Ala Met Glu Val	
	180 185 190	
5	gtg aaa ttt gtg aac ttt ctg ttg gtg aac ggc ttc caa act gcg att	624
	Val Lys Phe Val Asn Phe Leu Leu Val Asn Gly Phe Gln Thr Ala Ile	
	195 200 205	
10	gac ata ttt gag gat aga atc cgg ggt att gat atc att aaa tgg atg	672
	Asp Ile Phe Glu Asp Arg Ile Arg Gly Ile Asp Ile Ile Lys Trp Met	
	210 215 220	
15	gag cgc tat ctt cga gat aag aca gtg atg ata atc gta gca atc agc	720
	Glu Arg Tyr Leu Arg Asp Lys Thr Val Met Ile Ile Val Ala Ile Ser	
	225 230 235 240	
20	ccc aaa tac aaa cag gat gtg gaa ggc gct gag tcg cag ctg gac gag	768
	Pro Lys Tyr Lys Gln Asp Val Glu Gly Ala Glu Ser Gln Leu Asp Glu	
	245 250 255	
	gac gag cat ggc tta cat act aag tac att cat cgg atg atg cag att	816
	Asp Glu His Gly Leu His Thr Lys Tyr Ile His Arg Met Met Gln Ile	
	260 265 270	
25	gag ttc ata agt cag gga agc atg aac ttc aga ttc atc cct gtg ctc	864
	Glu Phe Ile Ser Gln Gly Ser Met Asn Phe Arg Phe Ile Pro Val Leu	
	275 280 285	
30	ttc cca aat gcc aag aag gag cat gtg ccg acc tgg ctt cag aac act	912
	Phe Pro Asn Ala Lys Lys Glu His Val Pro Thr Trp Leu Gln Asn Thr	
	290 295 300	
35	cat gtt tac agc tgg ccc aag aat aag aaa aac atc ctg ctg cgg ctg	960
	His Val Tyr Ser Trp Pro Lys Asn Lys Lys Asn Ile Leu Leu Arg Leu	
	305 310 315 320	
40	ctc agg gag gaa gag tat gtg gct cct ccc cga ggc cct ctg ccc acc	1008
	Leu Arg Glu Glu Glu Tyr Val Ala Pro Pro Arg Gly Pro Leu Pro Thr	
	325 330 335	
	ctt cag gtg gta ccc ttg tgacgatggc cactccagct cagtgccagc	1056
	Leu Gln Val Val Pro Leu	
	340	
45	ctgttctcac agcattcttc tagcggagct ggctggtggc acccaggccc tggaacacct	1116
	cttctacaga gtcctctgtc tcctgagtct gagttgtcct cgctgggctt ccagagcttc	1176
50	agtgcctgga tgctgcaggt gacagaaaca aacatctatg accacaaaaa ctctcatcac	1236
	ttcagctact tttatgagtc ggtcagatgc tctgtgtcct tagaccagtc taaatcatgc	1296
	tcaaataata aaatgattat tctttgt	1323
55	QDLPGPLRSRELPPQFELERYPMNAQLLPHPSPQAPWNCQYYCPGGPYHHQVPHGHGYPPAAAYQQVLQPA LPGQVLPGARARGPRPVQKVILNDSSPDQEERPAQRDFSFPRLPRDQLYRPPSNGVEAPEESLDLPAELRP HGPQAPSLAAVPRPPSNPLARGTLRTSNLPEELRKVFITYSMDTAMEVVKFVNFLVNGFQTAIDIFEDRIR GIDI IKWMERYLRDKTVMIIVAISP KYKQDVEGAESQLDEDEHGLHTKYIHRMMQIEFISQGS MNFRFIPVL FPNAKKEHVPTWLQNTHVYSWPKNKKNILLRLLREEEYVAPPRGPLPTLQVVPL.	

Reverse translation of rodent, e.g., mouse, DCRS6 (SEQ ID NO: 27):

5   cargayytnc cnggnccnyt nmgnwsnmgn garytncnc cncarttyga rytngarmgn 60  
      tayccnatga aygcncaryt nytncncncn cayccnwsnc cncargcncc ntggaaytgy 120  
      cartaytayt gyccnggngg nccntaycay caycargtnc cncayggnga yggntayccn 180  
 10   ccngcngcng cntaycarca rgtnytncar ccngcnytn cnggncargt nytncenggn 240  
      gcnmgngcnm gnggnccnmg nccngtnear aargtnathy tnaaygayws nwsnccncar 300  
 15   gaycargarg armgnccngc ncarmngay ttywsnttyc cnmgnytncc nmngnaycar 360  
      ytntaymgnc cncnwsnaa yggngtnar gcnccngarg arwsnytn ga yytnccngcn 420  
      garytnmgnc cncayggnc ncargcnccn wsnytnngcng cngtnccnmg nccnccnwsn 480  
 20   aayccnytn cnmnggnac nytnmgnacn wsnaayytnc cngargaryt nmgnaargtn 540  
      ttyathacnt aywsnatgga yacngcnatg gargtngt na arttygt naa yttyytnytn 600  
 25   gt naayggnt tyacaracngc nathgayath ttygargaym gnathmgngg nathgayath 660  
      athaartgga tggarmgnta yytnmgngay aaraengtna tgathathgt ngcnathwsn 720  
      ccnaartaya arcargaygt ngarggngcn garwsncary tngaygarga ygarca ygg 780  
 30   ytncayacna artayathca ymgnatgatg carathgart tyathwsnca rggnwsnatg 840  
      aayttymgnt tyathccngt nytnttyccn aaygcnaara argarcaygt nccnacntgg 900  
 35   ytncaraaya cncaygtnta ywsntggccn aaraayaara araayathyt nytnmgnytn 960  
      yt nmngngarg argartaygt ngcnccncn mgnggncny tncnacnytn ncargtngt 1020  
      ccnytn 1026  
 40

Table 6: Alignment of the cytoplasmic portions of various cytokine receptor subunits. The IL-17R\_Hu (SEQ ID NO: 28) is GenBank AAB99730.1(U58917), gi|7657230; the IL-17R\_Mu (SEQ ID NO: 29) is GenBank AAC52357.1(U31993), gi|6680411; the IL-17R\_Ce (SEQ ID NO: 30) is GenBank AAA811100.1(U39997), gi|1353171; and the DCRS6\_Ce (SEQ ID NO: 31) is EMBCAA90543.1(Z50177), gi|7503597. Of particular interest are motifs or features corresponding, in primate DCRS8 to: R/K at 339/340; D/E at 348/349; alpha helical regions from H353-Q365, C370-S381, E389-H396, K410-D414, and D485-H495; beta sheet regions correspond to F400-V404 and F458-Y462; E at 431; E/D at 442/443; Y/F at 458; D/E at 468-470; Y/F at 481; and Q/R/F at 523.

5	DCRS7_Mu DCRS7_Hu IL-17R_Hu IL-17R_Mu DCRS10 DCRS10_Mu DCRS9_Hu DCRS8_Hu 10 IL-17R_Ce DCRS6_Hu DCRS6_Ce	RTALLLSADG-AGYERLVGALASALSQMP---LRVAVDLWSRRE-LSAHGALAWFHHQR RAALLLYSADD-SGFERLVGALASALCQLP---LRVAVDLWSRRE-LSAQGPVAFWHAQR RKVWIIYSADH-PLYVDVVLKFAQFLLTACG--TEVALDLLEEQA-ISEAGVMTWVGRQK RKVWIVYSADH-PLYVEVVLKFAQFLITACG--TEVALDLLEEQA-ISEVGVMTWVSRQK RKVFITYSMD---TAMEVVKFVNFLLVNG---FQTAIDIFEDR--IRGIDI IKWMERYL RKVFITYSMD---TAMEVVKFVNFLLVNG---FQTAIDIFEDR--IRGIDI IKWMERYL RPVLLLHAADS-EAQRRLVGALAE LLRAALGGGRDVIVDLWEGRH-VARVGPLPWLWAAR PKVFLCYSSKDGQNHMNVVQCFAYFLQDFCG--CEVALDLWEDFS-LCREGQREWVIQKI VKVMIVYADDN-DLHTDCVKKLVENLRNCAS--CDPVFDLEKLI--TAEIVPSRWLVLDQI IKVLVVYPSEI--CFHHTICYFTEFLQNHCR--SEVILEKWQKKK-IAEMGPVQWLATQK FKVMLVCPEVS-GRDEDFMMRIADALKKSN--NKVVCDRWFEDSKNAEENMLHWVYEQT .: . : : *
15	DCRS7_Mu DCRS7_Hu IL-17R_Hu IL-17R_Mu DCRS10 20 DCRS10_Mu DCRS9_Hu DCRS8_Hu IL-17R_Ce DCRS6_Hu 25 DCRS6_Ce	RRILQEGGVVILLFSPAAVAQCQ---QWLQLQTVEP---GP---HDLA AAWLSCVLPDFL RQTLQEGGVVILLFSPGAVALCS---EWLQDGVSGPGAHP---HDAFRASLSCVLPDFL QEMVESNSKIIIVLCSRGTQAKWQALLGRGAP-VRLRCDHGKPV-GDLFTAAMNMILPDFK QEMVESNSKIIILCSRGTQAKWKAILGWAEPVQLRCDHWKPA-GDLFTAAMNMILPDFK R---DKTVMIIVAISPKYKQDVE---GAESQLDED-EHGL---HTKYIHRM-MQIEFIK R---DKTVMIIVAISPKYKQDVE---GAESQLDED-EHGL---HTKYIHRM-MQIEFIK TRVAREQGTVLLLWSGADLRPVVS---GPD-RAAP-----LLA---LLHAAP H---ESQFIIVVCSKGMKYFVD---KKNYKHKGGRGSGK---GELFLVAVSAIAEKL R S---SLKKFIIVVSDCAEKILD---TEASETHQLVQARP--FADLFGPAMEMIIRDAT K---AADKVVFLLSNDVNSVCD---GTCGKSEGSPSENS---QDLFPLAFNLFCSDLR K---IAEKIIVFHSAYYHPRCG---IYDVINNFFPCTDPR-----LAHIALT---PEAQ .: . *
30	DCRS7_Mu DCRS7_Hu IL-17R_Hu IL-17R_Mu DCRS10 DCRS10_Mu DCRS9_Hu 35 DCRS8_Hu IL-17R_Ce DCRS6_Hu DCRS6_Ce	QGRATGR-----YVG VYFDGLLHPDSVPSPFRVAPLFSLP-SQLPAFLDALQ--GGCSTS QGRAPGS-----YVGACFDRLLHPDAVPALFRTVPVFTLP-SQLPDLFGALQ--QPRAPR RPACFGT-----YVVCYFSEVSCDGDVDPDLFGAAPRYPLM-DRFEEVYFRIQ--DLEMFO RPACFGT-----YVVCYFSGICSERDVPDLFNITSRYPLM-DRFEEVYFRIQ--DLEMFE QGSMNFR-----FIPVLFPNAK-KEHVPTWLQNTHVYSWP-KNKKNILLRLL-REEEYVA QGSMNFR-----FIPVLFPNAK-KEHVPTWLQNTHVYSWP-KNKKNILLRLL-REEEYVA RPL-----LLLAYFSRLCAKGDIPPLRALPRYRL-RLDPLRLRALD--ARPF AE QAKQSSAALS KFI AVYFDYSC-EGDVPGILDSTKYRLM-DNLPQLCSHLHSRDHGLQE HNFPEAR---KKYAVVRFNYS P---HVPPNLA ILNLPTFIPEQFAQLTAFLHN-VEHTER SQIHLHK-----YVVYFREID-TKDDYNALSVCPKYHLM-KDATAFCAELL--HVKQQ RSVPKEV---EYVLP RDQKLL--EDAFDITIADPLVIDIPIEDVAIPENVP--IHHE SC
40	DCRS7_Mu DCRS7_Hu IL-17R_Hu IL-17R_Mu 45 DCRS10 DCRS10_Mu DCRS9_Hu DCRS8_Hu IL-17R_Ce 50 DCRS6_Hu DCRS6_Ce	AGRPAD RVER-----VT---QALRSALDSCTS----- SGRLQERAEQ-----VS---RALQPALDSYFHPP----- PGRMHRVGELSGDNYLRS---PGGRQLRAALDRFRDWQVRC PDW PGRMHVRELTDGNYLQS---PSGRQLKEAVLRFQEWQTQCPDW P----PRGPL-----PTLQVVPL----- P----PRGPL-----PTLQVVPL----- ATSWGRLGAR-----QRRQSRLELCSR----- PGQHTRQGSR-----RNYFRSKSGRSLYVAICNMHQFIDEFPDW ANVTQNISEA-----Q-----IHEWNL CASRMMSFFVRNPW VS---AGKR-----SQACHDGCCSL----- DSIDSRNNSK-----THSTDSGVSSLSS---NS--

Table 6 shows comparison of the available sequences of primate, rodent, and various other receptors. Various conserved residues are aligned and indicated. The structurally homologous cytoplasmic domains most likely signal through pathways like IL-17, e.g., through NFkB. Similar to IL-1 signalling, it is likely that these receptors are involved in innate immunity and/or development.

As used herein, the term DCRS shall be used to describe a protein comprising amino acid sequences shown in Tables 1-5, respectively. In many cases, a substantial fragment thereof will be functionally or structurally equivalent, including, e.g., an extracellular or intracellular domain. The invention also includes a protein variation of the respective DCRS allele whose sequence is provided, e.g., a mutein or soluble extracellular construct. Typically, such agonists or antagonists will exhibit less than about 10% sequence differences, and thus will often have between 1 and 11 substitutions, e.g., 2-, 3-, 5-, 7-fold, and others. It also encompasses allelic and other variants, e.g., natural polymorphic, of the protein described. Typically, it will bind to its corresponding biological ligand, perhaps in a dimerized state with an alpha receptor subunit, with high affinity, e.g., at least about 100 nM, usually better than about 30 nM, preferably better than about 10 nM, and more preferably at better than about 3 nM. The term shall also be used herein to refer to related naturally occurring forms, e.g., alleles, polymorphic variants, and metabolic variants of the mammalian protein. Preferred forms of the receptor complexes will bind the appropriate ligand with an affinity and selectivity appropriate for a ligand-receptor interaction.

This invention also encompasses combinations of proteins or peptides having substantial amino acid sequence identity with an amino acid sequence in Tables 1-5. It will include sequence variants with relatively few residue substitutions, e.g., preferably less than about 3-5.

A substantial polypeptide "fragment", or "segment", is a stretch of amino acid residues of at least about 8 amino acids, generally at least 10 amino acids, more generally at least 12 amino acids, often at least 14 amino acids, more often at least 16 amino acids, typically at least 18 amino acids, more typically at least 20 amino acids, usually at least 22 amino acids, more usually at least 24 amino acids, preferably at least 26 amino acids, more preferably at least 28 amino acids, and, in particularly preferred embodiments, at least about 30 or more amino acids. This includes, e.g., 40, 50, 60, 70, 85, 100, 115, 130, 150, and other lengths. Sequences of segments of different proteins can be compared to one another over appropriate length stretches, typically between conserved motifs. In many situations, fragments may exhibit functional properties of the intact subunits, e.g., the extracellular domain of the transmembrane receptor may retain the ligand binding features, and may be used to prepare a soluble receptor-like complex.

Amino acid sequence homology, or sequence identity, is determined by optimizing residue matches. In some comparisons, gaps may be introduced, as required. See, e.g., Needleham, et al., (1970) J. Mol. Biol. 48:443-453; Sankoff, et al., (1983) chapter one in Time Warps, String Edits, and Macromolecules: The Theory and Practice of Sequence Comparison, Addison-Wesley, Reading, MA; and software packages from IntelliGenetics, Mountain View, CA; and the University of Wisconsin Genetics Computer Group (GCG), Madison, WI; each of which is incorporated herein by reference. This changes when considering conservative substitutions as matches. Conservative substitutions typically include substitutions within the following groups: glycine, alanine; valine, isoleucine, leucine; aspartic acid, glutamic acid; asparagine, glutamine; serine, threonine; lysine, arginine; and phenylalanine, tyrosine. Homologous amino acid sequences are intended to include natural allelic and interspecies variations in the cytokine sequence. Typical homologous proteins or peptides will have from 50-100% homology (if gaps can be introduced), to 60-100% homology (if conservative substitutions are included) with an amino acid sequence segment of, e.g., Table 3 or 4. Homology measures will be at least about 70%, generally at least 76%, more generally at least 81%, often at least 85%, more often at least 88%, typically at least 90%, more typically at least 92%, usually at least 94%, more usually at least 95%, preferably at least 96%, and more preferably at least 97%, and in particularly preferred embodiments, at least 98% or more. The degree of homology will vary with the length of the compared segments. Homologous proteins or peptides, such as the allelic variants, will share most biological activities with the embodiments described in Tables 1-5.

As used herein, the term "biological activity" is used to describe, without limitation, effects on inflammatory responses, innate immunity, and/or morphogenic development by cytokine-like ligands. For example, these receptors should mediate phosphatase or phosphorylase activities, which activities are easily measured by standard procedures. See, e.g., Hardie, et al. (eds. 1995) The Protein Kinase FactBook vols. I and II, Academic Press, San Diego, CA; Hanks, et al. (1991) Meth. Enzymol. 200:38-62; Hunter, et al. (1992) Cell 70:375-388; Lewin (1990) Cell 61:743-752; Pines, et al. (1991) Cold Spring Harbor Symp. Quant. Biol. 56:449-463; and Parker, et al. (1993) Nature 363:736-738. The receptors, or portions thereof, may be useful as phosphate labeling enzymes to label general or specific substrates. The subunits may also be functional immunogens to elicit recognizing antibodies, or antigens capable of binding antibodies.

The terms ligand, agonist, antagonist, and analog of, e.g., a DCRS8 or DCRS9, include molecules that modulate the characteristic cellular responses to cytokine ligand proteins, as well as molecules possessing the more standard structural binding competition features of ligand-receptor interactions, e.g., where the receptor is a natural

receptor or an antibody. The cellular responses likely are typically mediated through receptor tyrosine kinase pathways.

Also, a ligand is a molecule which serves either as a natural ligand to which said receptor, or an analog thereof, binds, or a molecule which is a functional analog of the natural ligand. The functional analog may be a ligand with structural modifications, or may be a wholly unrelated molecule which has a molecular shape which interacts with the appropriate ligand binding determinants. The ligands may serve as agonists or antagonists, see, e.g., Goodman, et al. (eds. 1990) Goodman & Gilman's: The Pharmacological Bases of Therapeutics, Pergamon Press, New York.

Rational drug design may also be based upon structural studies of the molecular shapes of a receptor or antibody and other effectors or ligands. See, e.g., Herz, et al. (1997) J. Recept. Signal Transduct. Res. 17:671-776; and Chaiken, et al. (1996) Trends Biotechnol. 14:369-375. Effectors may be other proteins which mediate other functions in response to ligand binding, or other proteins which normally interact with the receptor. One means for determining which sites interact with specific other proteins is a physical structure determination, e.g., x-ray crystallography or 2 dimensional NMR techniques. These will provide guidance as to which amino acid residues form molecular contact regions. For a detailed description of protein structural determination, see, e.g., Blundell and Johnson (1976) Protein Crystallography, Academic Press, New York, which is hereby incorporated herein by reference.

## II. Activities

The cytokine receptor-like proteins will have a number of different biological activities, e.g., modulating cell proliferation, or in phosphate metabolism, being added to or removed from specific substrates, typically proteins. Such will generally result in modulation of an inflammatory function, other innate immunity response, or a morphological effect. The subunit will probably have a specific low affinity binding to the ligand.

The DCRS8 and DCRS9 have characteristic motifs of receptors signaling through the JAK pathway. See, e.g., Ihle, et al. (1997) Stem Cells 15(suppl. 1):105-111; Silvennoinen, et al. (1997) APMIS 105:497-509; Levy (1997) Cytokine Growth Factor Review 8:81-90; Winston and Hunter (1996) Current Biol. 6:668-671; Barrett (1996) Baillieres Clin. Gastroenterol. 10:1-15; and Briscoe, et al. (1996) Philos. Trans. R. Soc. Lond. B. Biol. Sci. 351:167-171.

The biological activities of the cytokine receptor subunits will be related to addition or removal of phosphate moieties to substrates, typically in a specific manner, but occasionally in a non specific manner. Substrates may be identified, or conditions for



enzymatic activity may be assayed by standard methods, e.g., as described in Hardie, et al. (eds. 1995) The Protein Kinase FactBook vols. I and II, Academic Press, San Diego, CA; Hanks, et al. (1991) Meth. Enzymol. 200:38-62; Hunter, et al. (1992) Cell 70:375-388; Lewin (1990) Cell 61:743-752; Pines, et al. (1991) Cold Spring Harbor Symp. Quant. Biol. 56:449-463; and Parker, et al. (1993) Nature 363:736-738.

The receptor subunits may combine to form functional complexes, e.g., which may be useful for binding ligand or preparing antibodies. These will have substantial diagnostic uses, including detection or quantitation.

### 10 III. Nucleic Acids

This invention contemplates use of isolated nucleic acid or fragments, e.g., which encode these or closely related proteins, or fragments thereof, e.g., to encode a corresponding polypeptide, preferably one which is biologically active. In addition, this invention covers isolated or recombinant DNAs which encode combinations of such  
15 proteins or polypeptides having characteristic sequences, e.g., of the DCRSs. Typically, the nucleic acid is capable of hybridizing, under appropriate conditions, with a nucleic acid sequence segment shown in Tables 1-5, but preferably not with a corresponding segment of other receptors described in Table 6. Said biologically active protein or polypeptide can be a full length protein, or fragment, and will typically have a segment of  
20 amino acid sequence highly homologous, e.g., exhibiting significant stretches of identity, to one shown in Tables 1-5. Further, this invention covers the use of isolated or recombinant nucleic acid, or fragments thereof, which encode proteins having fragments which are equivalent to the DCRS8 or DCRS9 proteins. The isolated nucleic acids can have the respective regulatory sequences in the 5' and 3' flanks, e.g., promoters,  
25 enhancers, poly-A addition signals, and others from the natural gene. Combinations, as described, are also provided.

An "isolated" nucleic acid is a nucleic acid, e.g., an RNA, DNA, or a mixed polymer, which is substantially pure, e.g., separated from other components which naturally accompany a native sequence, such as ribosomes, polymerases, and flanking  
30 genomic sequences from the originating species. The term embraces a nucleic acid sequence which has been removed from its naturally occurring environment, and includes recombinant or cloned DNA isolates, which are thereby distinguishable from naturally occurring compositions, and chemically synthesized analogs or analogs biologically synthesized by heterologous systems. A substantially pure molecule includes isolated  
35 forms of the molecule, either completely or substantially pure.

An isolated nucleic acid will generally be a homogeneous composition of molecules, but will, in some embodiments, contain heterogeneity, preferably minor. This

heterogeneity is typically found at the polymer ends or portions not critical to a desired biological function or activity.

A "recombinant" nucleic acid is typically defined either by its method of production or its structure. In reference to its method of production, e.g., a product made by a process, the process is use of recombinant nucleic acid techniques, e.g., involving human intervention in the nucleotide sequence. Typically this intervention involves in vitro manipulation, although under certain circumstances it may involve more classical animal breeding techniques. Alternatively, it can be a nucleic acid made by generating a sequence comprising fusion of two fragments which are not naturally contiguous to each other, but is meant to exclude products of nature, e.g., naturally occurring mutants as found in their natural state. Thus, for example, products made by transforming cells with an unnaturally occurring vector is encompassed, as are nucleic acids comprising sequence derived using any synthetic oligonucleotide process. Such a process is often done to replace a codon with a redundant codon encoding the same or a conservative amino acid, while typically introducing or removing a restriction enzyme sequence recognition site. Alternatively, the process is performed to join together nucleic acid segments of desired functions to generate a single genetic entity comprising a desired combination of functions not found in the commonly available natural forms, e.g., encoding a fusion protein. Restriction enzyme recognition sites are often the target of such artificial manipulations, but other site specific targets, e.g., promoters, DNA replication sites, regulation sequences, control sequences, or other useful features may be incorporated by design. A similar concept is intended for a recombinant, e.g., fusion, polypeptide. This will include a dimeric repeat. Specifically included are synthetic nucleic acids which, by genetic code redundancy, encode equivalent polypeptides to fragments of DCRSs and fusions of sequences from various different related molecules, e.g., other cytokine receptor family members.

A "fragment" in a nucleic acid context is a contiguous segment of at least about 17 nucleotides, generally at least 21 nucleotides, more generally at least 25 nucleotides, ordinarily at least 30 nucleotides, more ordinarily at least 35 nucleotides, often at least 39 nucleotides, more often at least 45 nucleotides, typically at least 50 nucleotides, more typically at least 55 nucleotides, usually at least 60 nucleotides, more usually at least 66 nucleotides, preferably at least 72 nucleotides, more preferably at least 79 nucleotides, and in particularly preferred embodiments will be at least 85 or more nucleotides. Typically, fragments of different genetic sequences can be compared to one another over appropriate length stretches, particularly defined segments such as the domains described below.

A nucleic acid which codes for the DCRS8 or DCRS9 will be particularly useful to identify genes, mRNA, and cDNA species which code for itself or closely related proteins, as well as DNAs which code for polymorphic, allelic, or other genetic variants, e.g., from different individuals or related species. Preferred probes for such screens are those regions of the interleukin which are conserved between different polymorphic variants or which contain nucleotides which lack specificity, and will preferably be full length or nearly so. In other situations, polymorphic variant specific sequences will be more useful.

This invention further covers recombinant nucleic acid molecules and fragments having a nucleic acid sequence identical to or highly homologous to the isolated DNA set forth herein. In particular, the sequences will often be operably linked to DNA segments which control transcription, translation, and DNA replication. These additional segments typically assist in expression of the desired nucleic acid segment.

Homologous, or highly identical, nucleic acid sequences, when compared to one another, e.g., DCRS8 sequences, exhibit significant similarity. The standards for homology in nucleic acids are either measures for homology generally used in the art by sequence comparison or based upon hybridization conditions. Comparative hybridization conditions are described in greater detail below.

Substantial identity in the nucleic acid sequence comparison context means either that the segments, or their complementary strands, when compared, are identical when optimally aligned, with appropriate nucleotide insertions or deletions, in at least about 60% of the nucleotides, generally at least 66%, ordinarily at least 71%, often at least 76%, more often at least 80%, usually at least 84%, more usually at least 88%, typically at least 91%, more typically at least about 93%, preferably at least about 95%, more preferably at least about 96 to 98% or more, and in particular embodiments, as high as about 99% or more of the nucleotides, including, e.g., segments encoding structural domains such as the segments described below. Alternatively, substantial identity will exist when the segments will hybridize under selective hybridization conditions, to a strand or its complement, typically using a sequence derived from Tables 1-5. Typically, selective hybridization will occur when there is at least about 55% homology over a stretch of at least about 14 nucleotides, more typically at least about 65%, preferably at least about 75%, and more preferably at least about 90%. See, Kanehisa (1984) Nucl. Acids Res. 12:203-213, which is incorporated herein by reference. The length of homology comparison, as described, may be over longer stretches, and in certain embodiments will be over a stretch of at least about 17 nucleotides, generally at least about 20 nucleotides, ordinarily at least about 24 nucleotides, usually at least about 28 nucleotides, typically at least about 32 nucleotides, more typically at least about 40 nucleotides, preferably at least

about 50 nucleotides, and more preferably at least about 75 to 100 or more nucleotides. This includes, e.g., 125, 150, 175, 200, 225, 246, 273, and other lengths.

Stringent conditions, in referring to homology in the hybridization context, will be stringent combined conditions of salt, temperature, organic solvents, and other parameters typically controlled in hybridization reactions. Stringent temperature conditions will usually include temperatures in excess of about 30 C, more usually in excess of about 37 C, typically in excess of about 45 C, more typically in excess of about 55 C, preferably in excess of about 65 C, and more preferably in excess of about 70 C. Stringent salt conditions will ordinarily be less than about 500 mM, usually less than about 400 mM, more usually less than about 300 mM, typically less than about 200 mM, preferably less than about 100 mM, and more preferably less than about 80 mM, even down to less than about 20 mM. However, the combination of parameters is much more important than the measure of any single parameter. See, e.g., Wetmur and Davidson (1968) J. Mol. Biol. 31:349-370, which is hereby incorporated herein by reference.

The isolated DNA can be readily modified by nucleotide substitutions, nucleotide deletions, nucleotide insertions, and inversions of nucleotide stretches. These modifications result in novel DNA sequences which encode this protein or its derivatives. These modified sequences can be used to produce mutant proteins (muteins) or to enhance the expression of variant species. Enhanced expression may involve gene amplification, increased transcription, increased translation, and other mechanisms. Such mutant DCRS8-like derivatives include predetermined or site-specific mutations of the protein or its fragments, including silent mutations using genetic code degeneracy. "Mutant DCRS8" as used herein encompasses a polypeptide otherwise falling within the homology definition of the DCRS8 as set forth above, but having an amino acid sequence which differs from that of other cytokine receptor-like proteins as found in nature, whether by way of deletion, substitution, or insertion. In particular, "site specific mutant DCRS8" encompasses a protein having substantial sequence identity with a protein of Table 3, and typically shares most of the biological activities or effects of the forms disclosed herein.

Although site specific mutation sites are predetermined, mutants need not be site specific. Mammalian DCRS8 mutagenesis can be achieved by making amino acid insertions or deletions in the gene, coupled with expression. Substitutions, deletions, insertions, or many combinations may be generated to arrive at a final construct. Insertions include amino- or carboxy- terminal fusions. Random mutagenesis can be conducted at a target codon and the expressed mammalian DCRS mutants can then be screened for the desired activity, providing some aspect of a structure-activity relationship. Methods for making substitution mutations at predetermined sites in DNA

having a known sequence are well known in the art, e.g., by M13 primer mutagenesis. See also Sambrook, et al. (1989) and Ausubel, et al. (1987 and periodic Supplements).

The mutations in the DNA normally should not place coding sequences out of reading frames and preferably will not create complementary regions that could hybridize to produce secondary mRNA structure such as loops or hairpins.

The phosphoramidite method described by Beaucage and Carruthers (1981) Tetra. Letts. 22:1859-1862, will produce suitable synthetic DNA fragments. A double stranded fragment will often be obtained either by synthesizing the complementary strand and annealing the strand together under appropriate conditions or by adding the complementary strand using DNA polymerase with an appropriate primer sequence.

Polymerase chain reaction (PCR) techniques can often be applied in mutagenesis. Alternatively, mutagenesis primers are commonly used methods for generating defined mutations at predetermined sites. See, e.g., Innis, et al. (eds. 1990) PCR Protocols: A Guide to Methods and Applications Academic Press, San Diego, CA; and Dieffenbach and Dveksler (1995; eds.) PCR Primer: A Laboratory Manual Cold Spring Harbor Press, CSH, NY.

Certain embodiments of the invention are directed to combination compositions comprising the receptor or ligand sequences described. In other embodiments, functional portions of the sequences may be joined to encode fusion proteins. In other forms, variants of the described sequences may be substituted.

#### IV. Proteins, Peptides

As described above, the present invention encompasses primate DCRS6-10, e.g., whose sequences are disclosed in Tables 1-5, and described above. Allelic and other variants are also contemplated, including, e.g., fusion proteins combining portions of such sequences with others, including, e.g., epitope tags and functional domains.

The present invention also provides recombinant proteins, e.g., heterologous fusion proteins using segments from these primate or rodent proteins. A heterologous fusion protein is a fusion of proteins or segments which are naturally not normally fused in the same manner. Thus, the fusion product of, e.g., a DCRS8 with another cytokine receptor is a continuous protein molecule having sequences fused in a typical peptide linkage, typically made as a single translation product and exhibiting properties, e.g., sequence or antigenicity, derived from each source peptide. A similar concept applies to heterologous nucleic acid sequences. Combinations of various designated proteins into complexes are also provided.

In addition, new constructs may be made from combining similar functional or structural domains from other related proteins, e.g., cytokine receptors or Toll-like

receptors, including species variants. For example, ligand-binding or other segments may be "swapped" between different new fusion polypeptides or fragments. See, e.g., Cunningham, et al. (1989) Science 243:1330-1336; and O'Dowd, et al. (1988) J. Biol. Chem. 263:15985-15992, each of which is incorporated herein by reference. Thus, new  
5 chimeric polypeptides exhibiting new combinations of specificities will result from the functional linkage of receptor-binding specificities. For example, the ligand binding domains from other related receptor molecules may be added or substituted for other domains of this or related proteins. The resulting protein will often have hybrid function and properties. For example, a fusion protein may include a targeting domain which may  
10 serve to provide sequestering of the fusion protein to a particular subcellular organelle.

Candidate fusion partners and sequences can be selected from various sequence data bases, e.g., GenBank, c/o IntelliGenetics, Mountain View, CA; and BCG, University of Wisconsin Biotechnology Computing Group, Madison, WI, which are each  
15 incorporated herein by reference. In particular, combinations of polypeptide sequences provided in Tables 1-5 are particularly preferred. Variant forms of the proteins may be substituted in the described combinations.

The present invention particularly provides muteins which bind cytokine-like ligands, and/or which are affected in signal transduction. Structural alignment of human DCRSs with other members of the cytokine receptor family show conserved  
20 features/residues. See Table 6. Alignment of the human DCRS8 sequence with other members of the cytokine receptor family indicates various structural and functionally shared features. See also, Bazan, et al. (1996) Nature 379:591; Lodi, et al. (1994) Science 263:1762-1766; Sayle and Milner-White (1995) TIBS 20:374-376; and Gronenberg, et al. (1991) Protein Engineering 4:263-269.

Substitutions with either mouse sequences or human sequences are particularly  
25 preferred. Conversely, conservative substitutions away from the ligand binding interaction regions will probably preserve most signaling activities; and conservative substitutions away from the intracellular domains will probably preserve most ligand binding properties.

"Derivatives" of the primate DCRS8 include amino acid sequence mutants, glycosylation variants, metabolic derivatives and covalent or aggregative conjugates with other chemical moieties. Covalent derivatives can be prepared by linkage of  
30 functionalities to groups which are found in the DCRS8 amino acid side chains or at the N- or C- termini, e.g., by means which are well known in the art. These derivatives can include, without limitation, aliphatic esters or amides of the carboxyl terminus, or of  
35 residues containing carboxyl side chains, O-acyl derivatives of hydroxyl group-containing residues, and N-acyl derivatives of the amino terminal amino acid or amino-group

containing residues, e.g., lysine or arginine. Acyl groups are selected from the group of alkyl-moieties, including C3 to C18 normal alkyl, thereby forming alkanoyl aroyl species.

5 In particular, glycosylation alterations are included, e.g., made by modifying the glycosylation patterns of a polypeptide during its synthesis and processing, or in further processing steps. Particularly preferred means for accomplishing this are by exposing the polypeptide to glycosylating enzymes derived from cells which normally provide such processing, e.g., mammalian glycosylation enzymes. Deglycosylation enzymes are also contemplated. Also embraced are versions of the same primary amino acid sequence  
10 which have other minor modifications, including phosphorylated amino acid residues, e.g., phosphotyrosine, phosphoserine, or phosphothreonine.

A major group of derivatives are covalent conjugates of the receptors or fragments thereof with other proteins of polypeptides. These derivatives can be synthesized in recombinant culture such as N- or C-terminal fusions or by the use of agents known in the art for their usefulness in cross-linking proteins through reactive side groups. Preferred  
15 derivatization sites with cross-linking agents are at free amino groups, carbohydrate moieties, and cysteine residues.

Fusion polypeptides between the receptors and other homologous or heterologous proteins are also provided. Homologous polypeptides may be fusions between different receptors, resulting in, for instance, a hybrid protein exhibiting binding specificity for  
20 multiple different cytokine ligands, or a receptor which may have broadened or weakened specificity of substrate effect. Likewise, heterologous fusions may be constructed which would exhibit a combination of properties or activities of the derivative proteins. Typical examples are fusions of a reporter polypeptide, e.g., luciferase, with a segment or domain of a receptor, e.g., a ligand-binding segment, so that the presence or location of a desired  
25 ligand may be easily determined. See, e.g., Dull, et al., U.S. Patent No. 4,859,609, which is hereby incorporated herein by reference. Other gene fusion partners include glutathione-S-transferase (GST), bacterial  $\beta$ -galactosidase, trpE, Protein A,  $\beta$ -lactamase, alpha amylase, alcohol dehydrogenase, and yeast alpha mating factor. See, e.g., Godowski, et al. (1988) Science 241:812-816. Labeled proteins will often be substituted  
30 in the described combinations of proteins.

The phosphoramidite method described by Beaucage and Carruthers (1981) Tetra. Letts. 22:1859-1862, will produce suitable synthetic DNA fragments. A double stranded fragment will often be obtained either by synthesizing the complementary strand and annealing the strand together under appropriate conditions or by adding the  
35 complementary strand using DNA polymerase with an appropriate primer sequence.

Such polypeptides may also have amino acid residues which have been chemically modified by phosphorylation, sulfonation, biotinylation, or the addition or removal of

other moieties, particularly those which have molecular shapes similar to phosphate groups. In some embodiments, the modifications will be useful labeling reagents, or serve as purification targets, e.g., affinity ligands.

5 Fusion proteins will typically be made by either recombinant nucleic acid methods or by synthetic polypeptide methods. Techniques for nucleic acid manipulation and expression are described generally, for example, in Sambrook, et al. (1989) Molecular Cloning: A Laboratory Manual (2d ed.), Vols. 1-3, Cold Spring Harbor Laboratory, and Ausubel, et al. (eds. 1987 and periodic supplements) Current Protocols in Molecular Biology, Greene/Wiley, New York, which are each incorporated herein by reference.

10 Techniques for synthesis of polypeptides are described, for example, in Merrifield (1963) J. Amer. Chem. Soc. 85:2149-2156; Merrifield (1986) Science 232: 341-347; and Atherton, et al. (1989) Solid Phase Peptide Synthesis: A Practical Approach, IRL Press, Oxford; each of which is incorporated herein by reference. See also Dawson, et al. (1994) Science 266:776-779 for methods to make larger polypeptides.

15 This invention also contemplates the use of derivatives of a DCRS8 other than variations in amino acid sequence or glycosylation. Such derivatives may involve covalent or aggregative association with chemical moieties. These derivatives generally fall into three classes: (1) salts, (2) side chain and terminal residue covalent modifications, and (3) adsorption complexes, for example with cell membranes. Such covalent or

20 aggregative derivatives are useful as immunogens, as reagents in immunoassays, or in purification methods such as for affinity purification of a receptor or other binding molecule, e.g., an antibody. For example, a cytokine ligand can be immobilized by covalent bonding to a solid support such as cyanogen bromide-activated Sepharose, by methods which are well known in the art, or adsorbed onto polyolefin surfaces, with or

25 without glutaraldehyde cross-linking, for use in the assay or purification of a cytokine receptor, antibodies, or other similar molecules. The ligand can also be labeled with a detectable group, for example radioiodinated by the chloramine T procedure, covalently bound to rare earth chelates, or conjugated to another fluorescent moiety for use in diagnostic assays.

30 A combination, e.g., including a DCRS8, of this invention can be used as an immunogen for the production of antisera or antibodies specific, e.g., capable of distinguishing between other cytokine receptor family members, for the combinations described. The complexes can be used to screen monoclonal antibodies or antigen-binding fragments prepared by immunization with various forms of impure preparations

35 containing the protein. In particular, the term "antibodies" also encompasses antigen binding fragments of natural antibodies, e.g., Fab, Fab2, Fv, etc. The purified DCRS8 can also be used as a reagent to detect antibodies generated in response to the presence of



elevated levels of expression, or immunological disorders which lead to antibody production to the endogenous receptor. Additionally, DCRS8 fragments may also serve as immunogens to produce the antibodies of the present invention, as described immediately below. For example, this invention contemplates antibodies having binding affinity to or being raised against the amino acid sequences shown in Tables 1-5, fragments thereof, or various homologous peptides. In particular, this invention contemplates antibodies having binding affinity to, or having been raised against, specific fragments which are predicted to be, or actually are, exposed at the exterior protein surface of the native DCRS8 or DCRS9. Complexes of combinations of proteins will also be useful, and antibody preparations thereto can be made.

The blocking of physiological response to the receptor ligands may result from the inhibition of binding of the ligand to the receptor, likely through competitive inhibition. Thus, in vitro assays of the present invention will often use antibodies or antigen binding segments of these antibodies, or fragments attached to solid phase substrates. These assays will also allow for the diagnostic determination of the effects of either ligand binding region mutations and modifications, or other mutations and modifications, e.g., which affect signaling or enzymatic function.

This invention also contemplates the use of competitive drug screening assays, e.g., where neutralizing antibodies to the receptor complexes or fragments compete with a test compound for binding to a ligand or other antibody. In this manner, the neutralizing antibodies or fragments can be used to detect the presence of a polypeptide which shares one or more binding sites to a receptor and can also be used to occupy binding sites on a receptor that might otherwise bind a ligand.

## V. Making Nucleic Acids and Protein

DNA which encodes the protein or fragments thereof can be obtained by chemical synthesis, screening cDNA libraries, or by screening genomic libraries prepared from a wide variety of cell lines or tissue samples. Natural sequences can be isolated using standard methods and the sequences provided herein, e.g., in Tables 1-5. Other species counterparts can be identified by hybridization techniques, or by various PCR techniques, combined with or by searching in sequence databases, e.g., GenBank.

This DNA can be expressed in a wide variety of host cells for the synthesis of a full-length receptor or fragments which can in turn, for example, be used to generate polyclonal or monoclonal antibodies; for binding studies; for construction and expression of modified ligand binding or kinase/phosphatase domains; and for structure/function studies. Variants or fragments can be expressed in host cells that are transformed or transfected with appropriate expression vectors. These molecules can be substantially

free of protein or cellular contaminants, other than those derived from the recombinant host, and therefore are particularly useful in pharmaceutical compositions when combined with a pharmaceutically acceptable carrier and/or diluent. The protein, or portions thereof, may be expressed as fusions with other proteins. Combinations of the described  
5 proteins, or nucleic acids encoding them, are particularly interesting.

Expression vectors are typically self-replicating DNA or RNA constructs containing the desired receptor gene or its fragments, usually operably linked to suitable genetic control elements that are recognized in a suitable host cell. These control elements are capable of effecting expression within a suitable host. The multiple genes  
10 may be coordinately expressed, and may be on a polycistronic message. The specific type of control elements necessary to effect expression will depend upon the eventual host cell used. Generally, the genetic control elements can include a prokaryotic promoter system or a eukaryotic promoter expression control system, and typically include a transcriptional promoter, an optional operator to control the onset of transcription,  
15 transcription enhancers to elevate the level of mRNA expression, a sequence that encodes a suitable ribosome binding site, and sequences that terminate transcription and translation. Expression vectors also usually contain an origin of replication that allows the vector to replicate independently of the host cell.

The vectors of this invention include those which contain DNA which encodes a  
20 combination of proteins, as described, or a biologically active equivalent polypeptide. The DNA can be under the control of a viral promoter and can encode a selection marker. This invention further contemplates use of such expression vectors which are capable of expressing eukaryotic cDNAs coding for such proteins in a prokaryotic or eukaryotic host, where the vector is compatible with the host and where the eukaryotic cDNAs are  
25 inserted into the vector such that growth of the host containing the vector expresses the cDNAs in question. Usually, expression vectors are designed for stable replication in their host cells or for amplification to greatly increase the total number of copies of the desirable gene per cell. It is not always necessary to require that an expression vector replicate in a host cell, e.g., it is possible to effect transient expression of the protein or its  
30 fragments in various hosts using vectors that do not contain a replication origin that is recognized by the host cell. It is also possible to use vectors that cause integration of the protein encoding portions into the host DNA by recombination.

Vectors, as used herein, comprise plasmids, viruses, bacteriophage, integratable DNA fragments, and other vehicles which enable the integration of DNA fragments into  
35 the genome of the host. Expression vectors are specialized vectors which contain genetic control elements that effect expression of operably linked genes. Plasmids are the most commonly used form of vector but all other forms of vectors which serve an equivalent

function and which are, or become, known in the art are suitable for use herein. See, e.g., Pouwels, et al. (1985 and Supplements) Cloning Vectors: A Laboratory Manual, Elsevier, N.Y., and Rodriguez, et al. (eds. 1988) Vectors: A Survey of Molecular Cloning Vectors and Their Uses, Butterworth, Boston, which are incorporated herein by reference.

5 Transformed cells are cells, preferably mammalian, that have been transformed or transfected with vectors constructed using recombinant DNA techniques. Transformed host cells usually express the desired proteins, but for purposes of cloning, amplifying, and manipulating its DNA, do not need to express the subject proteins. This invention further contemplates culturing transformed cells in a nutrient medium, thus permitting the  
10 proteins to accumulate. The proteins can be recovered, either from the culture or, in certain instances, from the culture medium.

For purposes of this invention, nucleic sequences are operably linked when they are functionally related to each other. For example, DNA for a presequence or secretory leader is operably linked to a polypeptide if it is expressed as a preprotein or participates  
15 in directing the polypeptide to the cell membrane or in secretion of the polypeptide. A promoter is operably linked to a coding sequence if it controls the transcription of the polypeptide; a ribosome binding site is operably linked to a coding sequence if it is positioned to permit translation. Usually, operably linked means contiguous and in reading frame, however, certain genetic elements such as repressor genes are not  
20 contiguously linked but still bind to operator sequences that in turn control expression.

Suitable host cells include prokaryotes, lower eukaryotes, and higher eukaryotes. Prokaryotes include both gram negative and gram positive organisms, e.g., E. coli and B. subtilis. Lower eukaryotes include yeasts, e.g., S. cerevisiae and Pichia, and species of the genus Dictyostelium. Higher eukaryotes include established tissue culture cell lines  
25 from animal cells, both of non-mammalian origin, e.g., insect cells, and birds, and of mammalian origin, e.g., human, primates, and rodents.

Prokaryotic host-vector systems include a wide variety of vectors for many different species. As used herein, E. coli and its vectors will be used generically to include equivalent vectors used in other prokaryotes. A representative vector for  
30 amplifying DNA is pBR322 or many of its derivatives. Vectors that can be used to express the receptor or its fragments include, but are not limited to, such vectors as those containing the lac promoter (pUC-series); trp promoter (pBR322-trp); Ipp promoter (the pIN-series); lambda-pP or pR promoters (pOTS); or hybrid promoters such as ptac (pDR540). See Brosius, et al. (1988) "Expression Vectors Employing Lambda-, trp-, lac-, and Ipp-derived Promoters", in Vectors: A Survey of Molecular Cloning Vectors and  
35 Their Uses, (eds. Rodriguez and Denhardt), Butterworth, Boston, Chapter 10, pp. 205-236, which is incorporated herein by reference.

Lower eukaryotes, e.g., yeasts and Dictyostelium, may be transformed with DCRS8 sequence containing vectors. For purposes of this invention, the most common lower eukaryotic host is the baker's yeast, Saccharomyces cerevisiae. It will be used to generically represent lower eukaryotes although a number of other strains and species are also available. Yeast vectors typically consist of a replication origin (unless of the integrating type), a selection gene, a promoter, DNA encoding the receptor or its fragments, and sequences for translation termination, polyadenylation, and transcription termination. Suitable expression vectors for yeast include such constitutive promoters as 3-phosphoglycerate kinase and various other glycolytic enzyme gene promoters or such inducible promoters as the alcohol dehydrogenase 2 promoter or metallothionine promoter. Suitable vectors include derivatives of the following types: self-replicating low copy number (such as the YRp-series), self-replicating high copy number (such as the YE<sub>p</sub>-series); integrating types (such as the YIp-series), or mini-chromosomes (such as the YC<sub>p</sub>-series).

Higher eukaryotic tissue culture cells are normally the preferred host cells for expression of the functionally active interleukin or receptor proteins. In principle, many higher eukaryotic tissue culture cell lines are workable, e.g., insect baculovirus expression systems, whether from an invertebrate or vertebrate source. However, mammalian cells are preferred. Transformation or transfection and propagation of such cells has become a routine procedure. Examples of useful cell lines include HeLa cells, Chinese hamster ovary (CHO) cell lines, baby rat kidney (BRK) cell lines, insect cell lines, bird cell lines, and monkey (COS) cell lines. Expression vectors for such cell lines usually include an origin of replication, a promoter, a translation initiation site, RNA splice sites (if genomic DNA is used), a polyadenylation site, and a transcription termination site. These vectors also usually contain a selection gene or amplification gene. Suitable expression vectors may be plasmids, viruses, or retroviruses carrying promoters derived, e.g., from such sources as from adenovirus, SV40, parvoviruses, vaccinia virus, or cytomegalovirus. Representative examples of suitable expression vectors include pCDNA1; pCD, see Okayama, et al. (1985) Mol. Cell Biol. 5:1136-1142; pMC1neo PolyA, see Thomas, et al. (1987) Cell 51:503-512; and a baculovirus vector such as pAC 373 or pAC 610.

For secreted proteins and some membrane proteins, an open reading frame usually encodes a polypeptide that consists of a mature or secreted product covalently linked at its N-terminus to a signal peptide. The signal peptide is cleaved prior to secretion of the mature, or active, polypeptide. The cleavage site can be predicted with a high degree of accuracy from empirical rules, e.g., von-Heijne (1986) Nucleic Acids Research 14:4683-4690; and Nielsen, et al. (1997) Protein Eng. 10:1-12, and the precise amino acid composition of the signal peptide often does not appear to be critical to its function, e.g.,

Randall, et al. (1989) Science 243:1156-1159; and Kaiser, et al. (1987) Science 235:312-317. The mature proteins of the invention can be readily determined using standard methods.

5 It will often be desired to express these polypeptides in a system which provides a specific or defined glycosylation pattern. In this case, the usual pattern will be that provided naturally by the expression system. However, the pattern will be modifiable by exposing the polypeptide, e.g., an unglycosylated form, to appropriate glycosylating proteins introduced into a heterologous expression system. For example, the receptor gene may be co-transformed with one or more genes encoding mammalian or other  
10 glycosylating enzymes. Using this approach, certain mammalian glycosylation patterns will be achievable in prokaryote or other cells. Expression in prokaryote cells will typically lead to unglycosylated forms of protein.

The source of DCRS8 can be a eukaryotic or prokaryotic host expressing recombinant DCRS8, such as is described above. The source can also be a cell line, but  
15 other mammalian cell lines are also contemplated by this invention, with the preferred cell line being from the human species.

Now that the sequences are known, the primate DCRS8 or DCRS9, fragments, or derivatives thereof can be prepared by conventional processes for synthesizing peptides. These include processes such as are described in Stewart and Young (1984) Solid Phase Peptide Synthesis, Pierce Chemical Co., Rockford, IL; Bodanszky and Bodanszky (1984) The Practice of Peptide Synthesis, Springer-Verlag, New York; and Bodanszky (1984) The Principles of Peptide Synthesis, Springer-Verlag, New York; all of each which are  
20 incorporated herein by reference. For example, an azide process, an acid chloride process, an acid anhydride process, a mixed anhydride process, an active ester process (for example, p-nitrophenyl ester, N-hydroxysuccinimide ester, or cyanomethyl ester), a carbodiimidazole process, an oxidative-reductive process, or a dicyclohexylcarbodiimide (DCCD)/additive process can be used. Solid phase and solution phase syntheses are both  
25 applicable to the foregoing processes. Similar techniques can be used with partial DCRS8 or DCRS9 sequences.

30 The DCRS8 proteins, fragments, or derivatives are suitably prepared in accordance with the above processes as typically employed in peptide synthesis, generally either by a so-called stepwise process which comprises condensing an amino acid to the terminal amino acid, one by one in sequence, or by coupling peptide fragments to the terminal amino acid. Amino groups that are not being used in the coupling reaction  
35 typically must be protected to prevent coupling at an incorrect location.

If a solid phase synthesis is adopted, the C-terminal amino acid is bound to an insoluble carrier or support through its carboxyl group. The insoluble carrier is not

particularly limited as long as it has a binding capability to a reactive carboxyl group. Examples of such insoluble carriers include halomethyl resins, such as chloromethyl resin or bromomethyl resin, hydroxymethyl resins, phenol resins, tert-alkyloxycarbonylhydrazidated resins, and the like.

5 An amino group-protected amino acid is bound in sequence through condensation of its activated carboxyl group and the reactive amino group of the previously formed peptide or chain, to synthesize the peptide step by step. After synthesizing the complete sequence, the peptide is split off from the insoluble carrier to produce the peptide. This solid-phase approach is generally described by Merrifield, et al. (1963) in J. Am. Chem.  
10 Soc. 85:2149-2156, which is incorporated herein by reference.

The prepared protein and fragments thereof can be isolated and purified from the reaction mixture by means of peptide separation, e.g., by extraction, precipitation, electrophoresis, various forms of chromatography, and the like. The receptors of this invention can be obtained in varying degrees of purity depending upon desired uses.

15 Purification can be accomplished by use of the protein purification techniques disclosed herein, see below, or by the use of the antibodies herein described in methods of immunoabsorbant affinity chromatography. This immunoabsorbant affinity chromatography is carried out by first linking the antibodies to a solid support and then contacting the linked antibodies with solubilized lysates of appropriate cells, lysates of  
20 other cells expressing the receptor, or lysates or supernatants of cells producing the protein as a result of DNA techniques, see below.

Generally, the purified protein will be at least about 40% pure, ordinarily at least about 50% pure, usually at least about 60% pure, typically at least about 70% pure, more typically at least about 80% pure, preferable at least about 90% pure and more preferably  
25 at least about 95% pure, and in particular embodiments, 97%-99% or more. Purity will usually be on a weight basis, but can also be on a molar basis. Different assays will be applied as appropriate. Individual proteins may be purified and thereafter combined.

## VI. Antibodies

30 Antibodies can be raised to the various mammalian, e.g., primate DCRS8 or DCRS9 proteins and fragments thereof, both in naturally occurring native forms and in their recombinant forms, the difference being that antibodies to the active receptor are more likely to recognize epitopes which are only present in the native conformations. Denatured antigen detection can also be useful in, e.g., Western analysis. Anti-idiotypic  
35 antibodies are also contemplated, which would be useful as agonists or antagonists of a natural receptor or an antibody.



Antibodies, including binding fragments and single chain versions, against predetermined fragments of the protein can be raised by immunization of animals with conjugates of the fragments with immunogenic proteins. Monoclonal antibodies are prepared from cells secreting the desired antibody. These antibodies can be screened for binding to normal or defective protein, or screened for agonistic or antagonistic activity. These monoclonal antibodies will usually bind with at least a  $K_D$  of about 1 mM, more usually at least about 300  $\mu$ M, typically at least about 100 $\mu$ M, more typically at least about 30  $\mu$ M, preferably at least about 10  $\mu$ M, and more preferably at least about 3  $\mu$ M or better.

The antibodies, including antigen binding fragments, of this invention can have significant diagnostic or therapeutic value. They can be potent antagonists that bind to the receptor and inhibit binding to ligand or inhibit the ability of the receptor to elicit a biological response, e.g., act on its substrate. They also can be useful as non-neutralizing antibodies and can be coupled to toxins or radionuclides to bind producing cells, or cells localized to the source of the interleukin. Further, these antibodies can be conjugated to drugs or other therapeutic agents, either directly or indirectly by means of a linker.

The antibodies of this invention can also be useful in diagnostic applications. As capture or non-neutralizing antibodies, they might bind to the receptor without inhibiting ligand or substrate binding. As neutralizing antibodies, they can be useful in competitive binding assays. They will also be useful in detecting or quantifying ligand. They may be used as reagents for Western blot analysis, or for immunoprecipitation or immunopurification of the respective protein. Likewise, nucleic acids and proteins may be immobilized to solid substrates for affinity purification or detection methods. The substrates may be, e.g., solid resin beads or sheets of plastic.

Protein fragments may be joined to other materials, particularly polypeptides, as fused or covalently joined polypeptides to be used as immunogens. Mammalian cytokine receptors and fragments may be fused or covalently linked to a variety of immunogens, such as keyhole limpet hemocyanin, bovine serum albumin, tetanus toxoid, etc. See (1969) Microbiology, Hoeber Medical Division, Harper and Row; Landsteiner (1962) Specificity of Serological Reactions, Dover Publications, New York; and Williams, et al. (1967) Methods in Immunology and Immunochemistry, Vol. 1, Academic Press, New York; each of which is incorporated herein by reference, for descriptions of methods of preparing polyclonal antisera. A typical method involves hyperimmunization of an animal with an antigen. The blood of the animal is then collected shortly after the repeated immunizations and the gamma globulin is isolated.

In some instances, it is desirable to prepare monoclonal antibodies from various mammalian hosts, such as mice, rodents, primates, humans, etc. Description of



techniques for preparing such monoclonal antibodies may be found in, e.g., Stites, et al. (eds.) Basic and Clinical Immunology (4th ed.), Lange Medical Publications, Los Altos, CA, and references cited therein; Harlow and Lane (1988) Antibodies: A Laboratory Manual, CSH Press; Goding (1986) Monoclonal Antibodies: Principles and Practice (2d ed.) Academic Press, New York; and particularly in Kohler and Milstein (1975) Nature 256:495-497, which discusses one method of generating monoclonal antibodies. Each of these references is incorporated herein by reference. Summarized briefly, this method involves injecting an animal with an immunogen. The animal is then sacrificed and cells taken from its spleen, which are then fused with myeloma cells. The result is a hybrid cell or "hybridoma" that is capable of reproducing in vitro. The population of hybridomas is then screened to isolate individual clones, each of which secrete a single antibody species to the immunogen. In this manner, the individual antibody species obtained are the products of immortalized and cloned single B cells from the immune animal generated in response to a specific site recognized on the immunogenic substance.

Other suitable techniques involve in vitro exposure of lymphocytes to the antigenic polypeptides or alternatively to selection of libraries of antibodies in phage or similar vectors. See, Huse, et al. (1989) "Generation of a Large Combinatorial Library of the Immunoglobulin Repertoire in Phage Lambda," Science 246:1275-1281; and Ward, et al. (1989) Nature 341:544-546, each of which is incorporated herein by reference. The polypeptides and antibodies of the present invention may be used with or without modification, including chimeric or humanized antibodies. Frequently, the polypeptides and antibodies will be labeled by joining, either covalently or non-covalently, a substance which provides for a detectable signal. A wide variety of labels and conjugation techniques are known and are reported extensively in both the scientific and patent literature. Suitable labels include radionuclides, enzymes, substrates, cofactors, inhibitors, fluorescent moieties, chemiluminescent moieties, magnetic particles, and the like. Patents, teaching the use of such labels include U.S. Patent Nos. 3,817,837; 3,850,752; 3,939,350; 3,996,345; 4,277,437; 4,275,149; and 4,366,241. Also, recombinant or chimeric immunoglobulins may be produced, see Cabilly, U.S. Patent No. 4,816,567; or made in transgenic mice, see Mendez, et al. (1997) Nature Genetics 15:146-156; Abgenix; and Medarex. These references are incorporated herein by reference.

The antibodies of this invention can also be used for affinity chromatography in isolating the DCRS8 proteins or peptides. Columns can be prepared where the antibodies are linked to a solid support, e.g., particles, such as agarose, Sephadex, or the like, where a cell lysate may be passed through the column, the column washed, followed by increasing concentrations of a mild denaturant, whereby the purified protein will be

released. Alternatively, the protein may be used to purify antibody. Appropriate cross absorptions or depletions may be applied.

5 The antibodies may also be used to screen expression libraries for particular expression products. Usually the antibodies used in such a procedure will be labeled with a moiety allowing easy detection of presence of antigen by antibody binding.

Antibodies raised against a cytokine receptor will also be used to raise anti-idiotypic antibodies. These will be useful in detecting or diagnosing various immunological conditions related to expression of the protein or cells which express the protein. They also will be useful as agonists or antagonists of the ligand, which may be competitive inhibitors or substitutes for naturally occurring ligands.

10 A cytokine receptor protein that specifically binds to or that is specifically immunoreactive with an antibody generated against a defined immunogen, such as an immunogen consisting of the amino acid sequence of SEQ ID NO: 14, is typically determined in an immunoassay. The immunoassay typically uses a polyclonal antiserum which was raised, e.g., to a protein of SEQ ID NO: 14. This antiserum is selected to have low crossreactivity against other cytokine receptor family members, preferably from the same species, and any such crossreactivity is removed by immunoabsorption prior to use in the immunoassay.

20 In order to produce antisera for use in an immunoassay, the protein, e.g., of SEQ ID NO: 14, is isolated as described herein. For example, recombinant protein may be produced in a mammalian cell line. An appropriate host, e.g., an inbred strain of mice such as Balb/c, is immunized with the selected protein, typically using a standard adjuvant, such as Freund's adjuvant, and a standard mouse immunization protocol (see Harlow and Lane, supra). Alternatively, a synthetic peptide derived from the sequences disclosed herein and conjugated to a carrier protein can be used as an immunogen.

25 Polyclonal sera are collected and titered against the immunogen protein in an immunoassay, e.g., a solid phase immunoassay with the immunogen immobilized on a solid support. Polyclonal antisera with a titer of  $10^4$  or greater are selected and tested for their cross reactivity against other cytokine receptor family members using a competitive binding immunoassay such as the one described in Harlow and Lane, supra, at pages 570-573. Preferably at least two cytokine receptor family members are used in this determination. These cytokine receptor family members can be produced as recombinant proteins and isolated using standard molecular biology and protein chemistry techniques as described herein.

35 Immunoassays in the competitive binding format can be used for the crossreactivity determinations. For example, the protein of SEQ ID NO: 14 can be immobilized to a solid support. Proteins added to the assay compete with the binding of

the antisera to the immobilized antigen. The ability of the above proteins to compete with the binding of the antisera to the immobilized protein is compared to the other proteins. The percent crossreactivity for the above proteins is calculated, using standard calculations. Those antisera with less than 10% crossreactivity with each of the proteins listed above are selected and pooled. The cross-reacting antibodies are then removed from the pooled antisera by immunoabsorption with the above-listed proteins.

The immunoabsorbed and pooled antisera are then used in a competitive binding immunoassay as described above to compare a second protein to the immunogen protein (e.g., the DCRS8 like protein of SEQ ID NO: 14). In order to make this comparison, the two proteins are each assayed at a wide range of concentrations and the amount of each protein required to inhibit 50% of the binding of the antisera to the immobilized protein is determined. If the amount of the second protein required is less than twice the amount of the protein of the selected protein or proteins that is required, then the second protein is said to specifically bind to an antibody generated to the immunogen.

It is understood that these cytokine receptor proteins are members of a family of homologous proteins that comprise at least 9 so far identified members, 6 mammalian and 3 worm embodiments. For a particular gene product, such as the DCRS8, the term refers not only to the amino acid sequences disclosed herein, but also to other proteins that are allelic, non-allelic, or species variants. It is also understood that the terms include nonnatural mutations introduced by deliberate mutation using conventional recombinant technology such as single site mutation, or by excising short sections of DNA encoding the respective proteins, or by substituting new amino acids, or adding new amino acids. Such minor alterations typically will substantially maintain the immunoidentity of the original molecule and/or its biological activity. Thus, these alterations include proteins that are specifically immunoreactive with a designated naturally occurring DCRS8 protein. The biological properties of the altered proteins can be determined by expressing the protein in an appropriate cell line and measuring the appropriate effect, e.g., upon transfected lymphocytes. Particular protein modifications considered minor would include conservative substitution of amino acids with similar chemical properties, as described above for the cytokine receptor family as a whole. By aligning a protein optimally with the protein of the cytokine receptors and by using the conventional immunoassays described herein to determine immunoidentity, one can determine the protein compositions of the invention.

## VII. Kits and quantitation

Both naturally occurring and recombinant forms of the cytokine receptor like molecules of this invention are particularly useful in kits and assay methods. For

example, these methods would also be applied to screening for binding activity, e.g., ligands for these proteins. Several methods of automating assays have been developed in recent years so as to permit screening of tens of thousands of compounds per year. See, e.g., a BIOMEK automated workstation, Beckman Instruments, Palo Alto, California, and  
5 Fodor, et al. (1991) Science 251:767-773, which is incorporated herein by reference. The latter describes means for testing binding by a plurality of defined polymers synthesized on a solid substrate. The development of suitable assays to screen for a ligand or agonist/antagonist homologous proteins can be greatly facilitated by the availability of large amounts of purified, soluble cytokine receptors in an active state such as is provided  
10 by this invention.

Purified protein can be coated directly onto plates for use in the aforementioned ligand screening techniques. However, non-neutralizing antibodies to these proteins can be used as capture antibodies to immobilize the respective receptor on the solid phase, useful, e.g., in diagnostic uses.

15 This invention also contemplates use of receptor subunit, fragments thereof, peptides, and their fusion products in a variety of diagnostic kits and methods for detecting the presence of the protein or its ligand. Alternatively, or additionally, antibodies against the molecules may be incorporated into the kits and methods. Typically the kit will have a compartment containing, e.g., a DCRS8 peptide or gene  
20 segment or a reagent which recognizes one or the other. Typically, recognition reagents, in the case of peptide, would be a receptor or antibody, or in the case of a gene segment, would usually be a hybridization probe.

A preferred kit for determining the concentration of DCRS8 in a sample would typically comprise a labeled compound, e.g., ligand or antibody, having known binding  
25 affinity for DCRS8, a source of DCRS8 (naturally occurring or recombinant) as a positive control, and a means for separating the bound from free labeled compound, e.g., a solid phase for immobilizing the DCRS8 in the test sample. Compartments containing reagents, and instructions, will normally be provided. Appropriate nucleic acid or protein containing kits are also provided.

30 Antibodies, including antigen binding fragments, specific for mammalian DCRS8 or a peptide fragment, or receptor fragments are useful in diagnostic applications to detect the presence of elevated levels of ligand and/or its fragments. Diagnostic assays may be homogeneous (without a separation step between free reagent and antibody-antigen complex) or heterogeneous (with a separation step). Various commercial assays exist,  
35 such as radioimmunoassay (RIA), enzyme-linked immunosorbent assay (ELISA), enzyme immunoassay (EIA), enzyme-multiplied immunoassay technique (EMIT), substrate-labeled fluorescent immunoassay (SLFIA) and the like. For example, unlabeled

antibodies can be employed by using a second antibody which is labeled and which recognizes the antibody to a cytokine receptor or to a particular fragment thereof. These assays have also been extensively discussed in the literature. See, e.g., Harlow and Lane (1988) Antibodies: A Laboratory Manual, CSH, and Coligan (ed. 1991 and periodic supplements) Current Protocols In Immunology Greene/Wiley, New York.

Anti-idiotypic antibodies may have similar use to serve as agonists or antagonists of cytokine receptors. These should be useful as therapeutic reagents under appropriate circumstances.

Frequently, the reagents for diagnostic assays are supplied in kits, so as to optimize the sensitivity of the assay. For the subject invention, depending upon the nature of the assay, the protocol, and the label, either labeled or unlabeled antibody, or labeled ligand is provided. This is usually in conjunction with other additives, such as buffers, stabilizers, materials necessary for signal production such as substrates for enzymes, and the like. Preferably, the kit will also contain instructions for proper use and disposal of the contents after use. Typically the kit has compartments for each useful reagent, and will contain instructions for proper use and disposal of reagents. Desirably, the reagents are provided as a dry lyophilized powder, where the reagents may be reconstituted in an aqueous medium having appropriate concentrations for performing the assay.

The aforementioned constituents of the diagnostic assays may be used without modification or may be modified in a variety of ways. For example, labeling may be achieved by covalently or non-covalently joining a moiety which directly or indirectly provides a detectable signal. In many of these assays, a test compound, cytokine receptor, or antibodies thereto can be labeled either directly or indirectly. Possibilities for direct labeling include label groups: radiolabels such as  $^{125}\text{I}$ , enzymes (U.S. Pat. No. 3,645,090) such as peroxidase and alkaline phosphatase, and fluorescent labels (U.S. Pat. No. 3,940,475) capable of monitoring the change in fluorescence intensity, wavelength shift, or fluorescence polarization. Both of the patents are incorporated herein by reference. Possibilities for indirect labeling include biotinylation of one constituent followed by binding to avidin coupled to one of the above label groups.

There are also numerous methods of separating the bound from the free ligand, or alternatively the bound from the free test compound. The cytokine receptor can be immobilized on various matrixes followed by washing. Suitable matrices include plastic such as an ELISA plate, filters, and beads. Methods of immobilizing the receptor to a matrix include, without limitation, direct adhesion to plastic, use of a capture antibody, chemical coupling, and biotin-avidin. The last step in this approach involves the precipitation of antibody/antigen complex by any of several methods including those

utilizing, e.g., an organic solvent such as polyethylene glycol or a salt such as ammonium sulfate. Other suitable separation techniques include, without limitation, the fluorescein antibody magnetizable particle method described in Rattle, et al. (1984) Clin. Chem. 30(9):1457-1461, and the double antibody magnetic particle separation as described in U.S. Pat. No. 4,659,678, each of which is incorporated herein by reference.

The methods for linking protein or fragments to various labels have been extensively reported in the literature and do not require detailed discussion here. Many of the techniques involve the use of activated carboxyl groups either through the use of carbodiimide or active esters to form peptide bonds, the formation of thioethers by reaction of a mercapto group with an activated halogen such as chloroacetyl, or an activated olefin such as maleimide, for linkage, or the like. Fusion proteins will also find use in these applications.

Another diagnostic aspect of this invention involves use of oligonucleotide or polynucleotide sequences taken from the sequence of an cytokine receptor. These sequences can be used as probes for detecting levels of the respective cytokine receptor in patients suspected of having an immunological disorder. The preparation of both RNA and DNA nucleotide sequences, the labeling of the sequences, and the preferred size of the sequences has received ample description and discussion in the literature. Normally an oligonucleotide probe should have at least about 14 nucleotides, usually at least about 18 nucleotides, and the polynucleotide probes may be up to several kilobases. Various labels may be employed, most commonly radionuclides, particularly  $^{32}\text{P}$ . However, other techniques may also be employed, such as using biotin modified nucleotides for introduction into a polynucleotide. The biotin then serves as the site for binding to avidin or antibodies, which may be labeled with a wide variety of labels, such as radionuclides, fluorescers, enzymes, or the like. Alternatively, antibodies may be employed which can recognize specific duplexes, including DNA duplexes, RNA duplexes, DNA-RNA hybrid duplexes, or DNA-protein duplexes. The antibodies in turn may be labeled and the assay carried out where the duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound to the duplex can be detected. The use of probes to the novel RNA may be carried out in conventional techniques such as nucleic acid hybridization, plus and minus screening, recombinational probing, hybrid released translation (HRT), and hybrid arrested translation (HART). Antisense nucleic acids, which may be used to block protein expression, are also provided. See, e.g., Isis Pharmaceuticals, Sequitur, Inc., or Hybridon. This also includes amplification techniques such as polymerase chain reaction (PCR).

Diagnostic kits which also test for the qualitative or quantitative presence of other markers are also contemplated. Diagnosis or prognosis may depend on the combination

of multiple indications used as markers. Thus, kits may test for combinations of markers. See, e.g., Viallet, et al. (1989) Progress in Growth Factor Res. 1:89-97.

#### VIII. Therapeutic Utility

5           This invention provides reagents with significant therapeutic value. See, e.g., Levitzki (1996) Curr. Opin. Cell Biol. 8:239-244. The cytokine receptors (naturally occurring or recombinant), fragments thereof, mutein receptors, and antibodies, along with compounds identified as having binding affinity to the receptors or antibodies, should be useful in the treatment of conditions exhibiting abnormal expression of the  
10           receptors of their ligands. Such abnormality will typically be manifested by immunological disorders, e.g., innate immunity, or developmentally. Additionally, this invention should provide therapeutic value in various diseases or disorders associated with abnormal expression or abnormal triggering of response to the ligand. For example, the IL-1 ligands have been suggested to be involved in morphologic development, e.g.,  
15           dorso-ventral polarity determination, and immune responses, particularly the primitive innate responses. See, e.g., Sun, et al. (1991) Eur. J. Biochem. 196:247-254; and Hultmark (1994) Nature 367:116-117.

          Recombinant cytokine receptors, muteins, agonist or antagonist antibodies thereto, or antibodies can be purified and then administered to a patient. These reagents can be  
20           combined for therapeutic use with additional active ingredients, e.g., in conventional pharmaceutically acceptable carriers or diluents, along with physiologically innocuous stabilizers and excipients. These combinations can be sterile, e.g., filtered, and placed into dosage forms as by lyophilization in dosage vials or storage in stabilized aqueous preparations. This invention also contemplates use of antibodies or binding fragments  
25           thereof which are not complement binding.

          Ligand screening using cytokine receptor or fragments thereof can be performed to identify molecules having binding affinity to the receptors. Subsequent biological assays can then be utilized to determine if a putative ligand can provide competitive binding, which can block intrinsic stimulating activity. Receptor fragments can be used  
30           as a blocker or antagonist in that it blocks the activity of ligand. Likewise, a compound having intrinsic stimulating activity can activate the receptor and is thus an agonist in that it simulates the activity of ligand, e.g., inducing signaling. This invention further contemplates the therapeutic use of antibodies to cytokine receptors as antagonists.

          The quantities of reagents necessary for effective therapy will depend upon many  
35           different factors, including means of administration, target site, reagent physiological life, pharmacological life, physiological state of the patient, and other medicants administered. Thus, treatment dosages should be titrated to optimize safety and efficacy. Typically,

dosages used in vitro may provide useful guidance in the amounts useful for in situ administration of these reagents. Animal testing of effective doses for treatment of particular disorders will provide further predictive indication of human dosage. Various considerations are described, e.g., in Gilman, et al. (eds. 1990) Goodman and Gilman's: The Pharmacological Bases of Therapeutics, 8th Ed., Pergamon Press; and Remington's Pharmaceutical Sciences, 17th ed. (1990), Mack Publishing Co., Easton, Penn.; each of which is hereby incorporated herein by reference. Methods for administration are discussed therein and below, e.g., for oral, intravenous, intraperitoneal, or intramuscular administration, transdermal diffusion, and others. Pharmaceutically acceptable carriers will include water, saline, buffers, and other compounds described, e.g., in the Merck Index, Merck & Co., Rahway, New Jersey. Because of the likely high affinity binding, or turnover numbers, between a putative ligand and its receptors, low dosages of these reagents would be initially expected to be effective. And the signaling pathway suggests extremely low amounts of ligand may have effect. Thus, dosage ranges would ordinarily be expected to be in amounts lower than 1 mM concentrations, typically less than about 10  $\mu$ M concentrations, usually less than about 100 nM, preferably less than about 10 pM (picomolar), and most preferably less than about 1 fM (femtomolar), with an appropriate carrier. Slow release formulations, or slow release apparatus will often be utilized for continuous administration.

Cytokine receptors, fragments thereof, and antibodies or its fragments, antagonists, and agonists, may be administered directly to the host to be treated or, depending on the size of the compounds, it may be desirable to conjugate them to carrier proteins such as ovalbumin or serum albumin prior to their administration. Therapeutic formulations may be administered in many conventional dosage formulations. While it is possible for the active ingredient to be administered alone, it is preferable to present it as a pharmaceutical formulation. Formulations comprise at least one active ingredient, as defined above, together with one or more acceptable carriers thereof. Each carrier must be both pharmaceutically and physiologically acceptable in the sense of being compatible with the other ingredients and not injurious to the patient. Formulations include those suitable for oral, rectal, nasal, or parenteral (including subcutaneous, intramuscular, intravenous and intradermal) administration. The formulations may conveniently be presented in unit dosage form and may be prepared by methods well known in the art of pharmacy. See, e.g., Gilman, et al. (eds. 1990) Goodman and Gilman's: The Pharmacological Bases of Therapeutics, 8th Ed., Pergamon Press; and Remington's Pharmaceutical Sciences, 17th ed. (1990), Mack Publishing Co., Easton, Penn.; Avis, et al. (eds. 1993) Pharmaceutical Dosage Forms: Parenteral Medications Dekker, NY; Lieberman, et al. (eds. 1990) Pharmaceutical Dosage Forms: Tablets Dekker, NY; and



Lieberman, et al. (eds. 1990) Pharmaceutical Dosage Forms: Disperse Systems Dekker, NY. The therapy of this invention may be combined with or used in association with other therapeutic agents, particularly agonists or antagonists of other cytokine receptor family members.

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## IX. Screening

Drug screening using DCRS8 or fragments thereof can be performed to identify compounds having binding affinity to the receptor subunit, including isolation of associated components. Subsequent biological assays can then be utilized to determine if the compound has intrinsic stimulating activity and is therefore a blocker or antagonist in that it blocks the activity of the ligand. Likewise, a compound having intrinsic stimulating activity can activate the receptor and is thus an agonist in that it simulates the activity of a cytokine ligand. This invention further contemplates the therapeutic use of antibodies to the receptor as cytokine agonists or antagonists.

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Similarly, complexes comprising multiple proteins may be used to screen for ligands or reagents capable of recognizing the complex. Most cytokine receptors comprise at least two subunits, which may be the same, or distinct. Alternatively, the transmembrane receptor may bind to a complex comprising a cytokine-like ligand associated with another soluble protein serving, e.g., as a second receptor subunit.

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One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant DNA molecules expressing the DCRS8 in combination with another cytokine receptor subunit. Cells may be isolated which express a receptor in isolation from other functional receptors. Such cells, either in viable or fixed form, can be used for standard antibody/antigen or ligand/receptor binding assays. See also, Parce, et al. (1989) Science 246:243-247; and Owicki, et al. (1990) Proc. Nat'l Acad. Sci. USA 87:4007-4011, which describe sensitive methods to detect cellular responses. Competitive assays are particularly useful, where the cells (source of putative ligand) are contacted and incubated with a labeled receptor or antibody having known binding affinity to the ligand, such as  $^{125}\text{I}$ -antibody, and a test sample whose binding affinity to the binding composition is being measured. The bound and free labeled binding compositions are then separated to assess the degree of ligand binding. The amount of test compound bound is inversely proportional to the amount of labeled receptor binding to the known source. Many techniques can be used to separate bound from free ligand to assess the degree of ligand binding. This separation step could typically involve a procedure such as adhesion to filters followed by washing, adhesion to plastic followed by washing, or centrifugation of the cell membranes. Viable cells could also be used to screen for the effects of drugs on cytokine mediated functions, e.g., second messenger

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levels, e.g.,  $\text{Ca}^{++}$ ; cell proliferation; inositol phosphate pool changes; and others. Some detection methods allow for elimination of a separation step, e.g., a proximity sensitive detection system. Calcium sensitive dyes will be useful for detecting  $\text{Ca}^{++}$  levels, with a fluorimeter or a fluorescence cell sorting apparatus.

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#### X. Ligands

The descriptions of the DCRS8 herein provides means to identify ligands, as described above. Such ligand should bind specifically to the respective receptor with reasonably high affinity. Various constructs are made available which allow either labeling of the receptor to detect its ligand. For example, directly labeling cytokine receptor, fusing onto it markers for secondary labeling, e.g., FLAG or other epitope tags, etc., will allow detection of receptor. This can be histological, as an affinity method for biochemical purification, or labeling or selection in an expression cloning approach. A two-hybrid selection system may also be applied making appropriate constructs with the available cytokine receptor sequences. See, e.g., Fields and Song (1989) Nature 340:245-246.

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Most likely candidates will be structurally related to members of the IL-17 family. See, e.g., USSN 09/480,287.

The broad scope of this invention is best understood with reference to the following examples, which are not intended to limit the inventions to the specific embodiments.

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### EXAMPLES

#### I. General Methods

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Some of the standard methods are described or referenced, e.g., in Maniatis, et al. (1982) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor Press; Sambrook, et al. (1989) Molecular Cloning: A Laboratory Manual, (2d ed.), vols. 1-3, CSH Press, NY; or Ausubel, et al. (1987 and Supplements) Current Protocols in Molecular Biology, Greene/Wiley, New York. Methods for protein purification include such methods as ammonium sulfate precipitation, column chromatography, electrophoresis, centrifugation, crystallization, and others. See, e.g., Ausubel, et al. (1987 and periodic supplements); Coligan, et al. (ed. 1996) and periodic supplements, Current Protocols In Protein Science Greene/Wiley, New York; Deutscher (1990) "Guide to Protein Purification" in Methods in Enzymology, vol. 182, and other volumes in this series; and manufacturer's literature on use of protein purification products, e.g., Pharmacia, Piscataway, N.J., or Bio-Rad, Richmond, CA. Combination

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with recombinant techniques allow fusion to appropriate segments, e.g., to a FLAG sequence or an equivalent which can be fused via a protease-removable sequence. See, e.g., Hochuli (1990) "Purification of Recombinant Proteins with Metal Chelate Absorbent" in Setlow (ed.) Genetic Engineering. Principle and Methods 12:87-98, Plenum Press, N.Y.; and Crowe, et al. (1992) OIAexpress: The High Level Expression & Protein Purification System QUIAGEN, Inc., Chatsworth, CA.

Computer sequence analysis is performed, e.g., using available software programs, including those from the GCG (U. Wisconsin) and GenBank sources. Public sequence databases were also used, e.g., from GenBank and others.

Many techniques applicable to IL-10 receptors may be applied to the DCRSs, as described, e.g., in USSN 08/110,683 (IL-10 receptor), which is incorporated herein by reference.

## II. Computational Analysis

Human sequences related to cytokine receptors were identified from genomic sequence database using, e.g., the BLAST server (Altschul, et al. (1994) Nature Genet. 6:119-129). Standard analysis programs may be used to evaluate structure, e.g., PHD (Rost and Sander (1994) Proteins 19:55-72) and DSC (King and Sternberg (1996) Protein Sci. 5:2298-2310). Standard comparison software includes, e.g., Altschul, et al. (1990) J. Mol. Biol. 215:403-10; Waterman (1995) Introduction to Computational Biology: Maps, Sequences, and Genomes Chapman & Hall; Lander and Waterman (eds. 1995) Calculating the Secrets of Life: Applications of the Mathematical Sciences in Molecular Biology National Academy Press; and Speed and Waterman (eds. 1996) Genetic Mapping and DNA Sequencing (IMA Volumes in Mathematics and Its Applications, Vol 81) Springer Verlag. Each reference is incorporate herein by reference.

## III. Cloning of full-length cDNAs; Chromosomal localization

PCR primers derived from the sequences are used to probe a human cDNA library. Sequences may be derived, e.g., from Tables 1-5, preferably those adjacent the ends of sequences. Full length cDNAs for primate, rodent, or other species DCRS8 are cloned, e.g., by DNA hybridization screening of  $\lambda$ gt10 phage. PCR reactions are conducted using T. aquaticus Taqplus DNA polymerase (Stratagene) under appropriate conditions. Extending partial length cDNA clones is typically routine.

Chromosome spreads are prepared. In situ hybridization is performed on chromosome preparations obtained from phytohemagglutinin-stimulated human lymphocytes cultured for 72 h. 5-bromodeoxyuridine was added for the final seven hours

of culture (60 µg/ml of medium), to ensure a posthybridization chromosomal banding of good quality.

A PCR fragment, amplified with the help of primers, is cloned into an appropriate vector. The vector is labeled by nick-translation with  $^3\text{H}$ . The radiolabeled probe is hybridized to metaphase spreads at final concentration of 200 ng/ml of hybridization solution as described, e.g., in Mattei, et al. (1985) Hum. Genet. 69:327-331.

After coating with nuclear track emulsion (KODAK NTB<sub>2</sub>), slides are exposed. To avoid any slipping of silver grains during the banding procedure, chromosome spreads are first stained with buffered Giemsa solution and metaphase photographed. R-banding is then performed by the fluorochrome-photolysis-Giemsa (FPG) method and metaphases rephotographed before analysis.

Similar appropriate methods are used for other species.

#### IV. Localization of mRNA

Human multiple tissue (Cat# 1, 2) and cancer cell line blots (Cat# 7757-1), containing approximately 2 µg of poly(A)<sup>+</sup> RNA per lane, are purchased from Clontech (Palo Alto, CA). Probes are radiolabeled with [ $\alpha$ - $^{32}\text{P}$ ] dATP, e.g., using the Amersham Rediprime random primer labeling kit (RPN1633). Prehybridization and hybridizations are performed, e.g., at 65° C in 0.5 M Na<sub>2</sub>HPO<sub>4</sub>, 7% SDS, 0.5 M EDTA (pH 8.0). High stringency washes are conducted, e.g., at 65° C with two initial washes in 2 x SSC, 0.1% SDS for 40 min followed by a subsequent wash in 0.1 x SSC, 0.1% SDS for 20 min. Membranes are then exposed at -70° C to X-Ray film (Kodak) in the presence of intensifying screens. More detailed studies by cDNA library Southernblots are performed with selected appropriate human DCRS clones to examine their expression in hemopoietic or other cell subsets.

Alternatively, two appropriate primers are selected from Tables 1-5. RT-PCR is used on an appropriate mRNA sample selected for the presence of message to produce a cDNA, e.g., a sample which expresses the gene.

Full length clones may be isolated by hybridization of cDNA libraries from appropriate tissues pre-selected by PCR signal. Northern blots can be performed.

Message for genes encoding DCRS will be assayed by appropriate technology, e.g., PCR, immunoassay, hybridization, or otherwise. Tissue and organ cDNA preparations are available, e.g., from Clontech, Mountain View, CA. Identification of sources of natural expression are useful, as described. And the identification of functional receptor subunit pairings will allow for prediction of what cells express the combination of receptor subunits which will result in a physiological responsiveness to each of the cytokine ligands.

For mouse counterpart distribution, e.g., Southern Analysis can be performed: DNA (5 µg) from a primary amplified cDNA library was digested with appropriate restriction enzymes to release the inserts, run on a 1% agarose gel and transferred to a nylon membrane (Schleicher and Schuell, Keene, NH).

5        Samples for mouse mRNA isolation may include: resting mouse fibroblastic L cell line (C200); Braf:ER (Braf fusion to estrogen receptor) transfected cells, control (C201); T cells, TH1 polarized (Mel14 bright, CD4+ cells from spleen, polarized for 7 days with IFN-γ and anti IL-4; T200); T cells, TH2 polarized (Mel14 bright, CD4+ cells from spleen, polarized for 7 days with IL-4 and anti-IFN-γ; T201); T cells, highly TH1  
10 polarized (see Openshaw, et al. (1995) J. Exp. Med. 182:1357-1367; activated with anti-CD3 for 2, 6, 16 h pooled; T202); T cells, highly TH2 polarized (see Openshaw, et al. (1995) J. Exp. Med. 182:1357-1367; activated with anti-CD3 for 2, 6, 16 h pooled; T203); CD44- CD25+ pre T cells, sorted from thymus (T204); TH1 T cell clone D1.1, resting for 3 weeks after last stimulation with antigen (T205); TH1 T cell clone D1.1, 10  
15 µg/ml ConA stimulated 15 h (T206); TH2 T cell clone CDC35, resting for 3 weeks after last stimulation with antigen (T207); TH2 T cell clone CDC35, 10 µg/ml ConA stimulated 15 h (T208); Mel14+ naive T cells from spleen, resting (T209); Mel14+ T cells, polarized to Th1 with IFN-γ/IL-12/anti-IL-4 for 6, 12, 24 h pooled (T210); Mel14+ T cells, polarized to Th2 with IL-4/anti-IFN-γ for 6, 13, 24 h pooled (T211); unstimulated  
20 mature B cell leukemia cell line A20 (B200); unstimulated B cell line CH12 (B201); unstimulated large B cells from spleen (B202); B cells from total spleen, LPS activated (B203); metrizamide enriched dendritic cells from spleen, resting (D200); dendritic cells from bone marrow, resting (D201); monocyte cell line RAW 264.7 activated with LPS 4 h (M200); bone-marrow macrophages derived with GM and M-CSF (M201); macrophage  
25 cell line J774, resting (M202); macrophage cell line J774 + LPS + anti-IL-10 at 0.5, 1, 3, 6, 12 h pooled (M203); macrophage cell line J774 + LPS + IL-10 at 0.5, 1, 3, 5, 12 h pooled (M204); aerosol challenged mouse lung tissue, Th2 primers, aerosol OVA challenge 7, 14, 23 h pooled (see Garlisi, et al. (1995) Clinical Immunology and Immunopathology 75:75-83; X206); Nippostrongylus-infected lung tissue (see Coffman,  
30 et al. (1989) Science 245:308-310; X200); total adult lung, normal (O200); total lung, rag-1 (see Schwarz, et al. (1993) Immunodeficiency 4:249-252; O205); IL-10 K.O. spleen (see Kuhn, et al. (1991) Cell 75:263-274; X201); total adult spleen, normal (O201); total spleen, rag-1 (O207); IL-10 K.O. Peyer's patches (O202); total Peyer's patches, normal (O210); IL-10 K.O. mesenteric lymph nodes (X203); total mesenteric lymph nodes,  
35 normal (O211); IL-10 K.O. colon (X203); total colon, normal (O212); NOD mouse pancreas (see Makino, et al. (1980) Jikken Dobutsu 29:1-13; X205); total thymus, rag-1 (O208); total kidney, rag-1 (O209); total heart, rag-1 (O202); total brain, rag-1 (O203);

total testes, rag-1 (O204); total liver, rag-1 (O206); rat normal joint tissue (O300); and rat arthritic joint tissue (X300).

Samples for human mRNA isolation may include, e.g.: peripheral blood mononuclear cells (monocytes, T cells, NK cells, granulocytes, B cells), resting (T100);  
 5 peripheral blood mononuclear cells, activated with anti-CD3 for 2, 6, 12 h pooled (T101); T cell, TH0 clone Mot 72, resting (T102); T cell, TH0 clone Mot 72, activated with anti-CD28 and anti-CD3 for 3, 6, 12 h pooled (T103); T cell, TH0 clone Mot 72, anergic treated with specific peptide for 2, 7, 12 h pooled (T104); T cell, TH1 clone HY06, resting (T107); T cell, TH1 clone HY06, activated with anti-CD28 and anti-CD3 for 3, 6,  
 10 12 h pooled (T108); T cell, TH1 clone HY06, anergic treated with specific peptide for 2, 6, 12 h pooled (T109); T cell, TH2 clone HY935, resting (T110); T cell, TH2 clone HY935, activated with anti-CD28 and anti-CD3 for 2, 7, 12 h pooled (T111); T cells CD4+CD45RO- T cells polarized 27 days in anti-CD28, IL-4, and anti IFN- $\gamma$ , TH2 polarized, activated with anti-CD3 and anti-CD28 4 h (T116); T cell tumor lines Jurkat  
 15 and Hut78, resting (T117); T cell clones, pooled AD130.2, Tc783.12, Tc783.13, Tc783.58, Tc782.69, resting (T118); T cell random  $\gamma\delta$  T cell clones, resting (T119); Splenocytes, resting (B100); Splenocytes, activated with anti-CD40 and IL-4 (B101); B cell EBV lines pooled WT49, RSB, JY, CVIR, 721.221, RM3, HSY, resting (B102); B cell line JY, activated with PMA and ionomycin for 1, 6 h pooled (B103); NK 20 clones  
 20 pooled, resting (K100); NK 20 clones pooled, activated with PMA and ionomycin for 6 h (K101); NKL clone, derived from peripheral blood of LGL leukemia patient, IL-2 treated (K106); NK cytotoxic clone 640-A30-1, resting (K107); hematopoietic precursor line TF1, activated with PMA and ionomycin for 1, 6 h pooled (C100); U937 premonocytic line, resting (M100); U937 premonocytic line, activated with PMA and ionomycin for 1,  
 25 6 h pooled (M101); elutriated monocytes, activated with LPS, IFN $\gamma$ , anti-IL-10 for 1, 2, 6, 12, 24 h pooled (M102); elutriated monocytes, activated with LPS, IFN $\gamma$ , IL-10 for 1, 2, 6, 12, 24 h pooled (M103); elutriated monocytes, activated with LPS, IFN $\gamma$ , anti-IL-10 for 4, 16 h pooled (M106); elutriated monocytes, activated with LPS, IFN $\gamma$ , IL-10 for 4, 16 h pooled (M107); elutriated monocytes, activated LPS for 1 h (M108); elutriated  
 30 monocytes, activated LPS for 6 h (M109); DC 70% CD1a+, from CD34+ GM-CSF, TNF $\alpha$  12 days, resting (D101); DC 70% CD1a+, from CD34+ GM-CSF, TNF $\alpha$  12 days, activated with PMA and ionomycin for 1 hr (D102); DC 70% CD1a+, from CD34+ GM-CSF, TNF $\alpha$  12 days, activated with PMA and ionomycin for 6 hr (D103); DC 95% CD1a+, from CD34+ GM-CSF, TNF $\alpha$  12 days FACS sorted, activated with PMA and  
 35 ionomycin for 1, 6 h pooled (D104); DC 95% CD14+, ex CD34+ GM-CSF, TNF $\alpha$  12 days FACS sorted, activated with PMA and ionomycin 1, 6 hr pooled (D105); DC CD1a+ CD86+, from CD34+ GM-CSF, TNF $\alpha$  12 days FACS sorted, activated with PMA and

ionomycin for 1, 6 h pooled (D106); DC from monocytes GM-CSF, IL-4 5 days, resting (D107); DC from monocytes GM-CSF, IL-4 5 days, resting (D108); DC from monocytes GM-CSF, IL-4 5 days, activated LPS 4, 16 h pooled (D109); DC from monocytes GM-CSF, IL-4 5 days, activated TNF $\alpha$ , monocyte supe for 4, 16 h pooled (D110); leiomyoma L11 benign tumor (X101); normal myometrium M5 (O115); malignant leiomyosarcoma GS1 (X103); lung fibroblast sarcoma line MRC5, activated with PMA and ionomycin for 1, 6 h pooled (C101); kidney epithelial carcinoma cell line CHA, activated with PMA and ionomycin for 1, 6 h pooled (C102); kidney fetal 28 wk male (O100); lung fetal 28 wk male (O101); liver fetal 28 wk male (O102); heart fetal 28 wk male (O103); brain fetal 28 wk male (O104); gallbladder fetal 28 wk male (O106); small intestine fetal 28 wk male (O107); adipose tissue fetal 28 wk male (O108); ovary fetal 25 wk female (O109); uterus fetal 25 wk female (O110); testes fetal 28 wk male (O111); spleen fetal 28 wk male (O112); adult placenta 28 wk (O113); and tonsil inflamed, from 12 year old (X100).

TaqMan quantitative PCR techniques have shown the DCRS6, in both mouse and human, to be expressed on T cells, including thymocytes and CD4<sup>+</sup> naive and differentiated (hDCRS6 is also expressed on dendritic cells), in gastrointestinal tissue, including stomach, intestine, colon and associated lymphoid tissue, e.g., Peyer's patches and mesenteric lymph nodes, and upregulated in inflammatory models of bowel disease, e.g., IL-10 KO mice. The hDCRS7 was detected in both resting and activated dendritic cells, epithelial cells, and mucosal tissues, including GI and reproductive tracts. These data suggest that family members are expressed in mucosal tissues and immune system cell types, and/or in gastrointestinal, airway, and reproductive tract development.

As such, therapeutic indications include, e.g., short bowel syndrome, post chemo/radio-therapy or alcoholic recovery, combinations with ulcer treatments or arthritis medication, Th2 pregnancy skewing, stomach lining/tissue regeneration, loss of adsorptive surface conditions, etc. See, e.g., Yamada, et al. (eds. 1999) Textbook of Gastroenterology; Yamada, et al. (eds. 1999) Textbook and Atlas of Gastroenterology; Gore and Levine (2000) Textbook of Gastrointestinal Radiology; and (1987) Textbook of Pediatric Gastroenterology.

Similar samples may isolated in other species for evaluation.

Primers specific for IL-17RA were designed and used in Taqman quantative PCR against various human libraries. IL-17RA is highly expressed in innate immune myeloid cells including dendritic cells and monocytes. Expression is also detected in T-cell libraries. These data demonstrate the receptor is expressed in immune cell types and may be regulated by activation conditions.

**Table for IL-17RA**  
**library description**

**CT for IL-  
17RA\_H**

DC ex monocytes GM-CSF, IL-4, resting	16.97
U937 premonocytic line, activated	17.14
DC ex monocytes GM-CSF, IL-4, resting	17.53
DC 70% CD1a+, ex CD34+ GM-CSF, TNFa, resting	18.17
monocytes, LPS, gIFN, anti-IL-10	18.27
DC ex monocytes GM-CSF, IL-4, LPS activated 4+16 hr	18.51
DC ex monocytes GM-CSF, IL-4, monokine activated 4+16 hr	18.68
kidney epithelial carcinoma cell line CHA, activated	18.69
monocytes, LPS, 1 hr	18.72
monocytes, LPS, 6 hr	18.72
DC 70% CD1a+, ex CD34+ GM-CSF, TNFa, activated 1 hr	18.91
DC 70% CD1a+, ex CD34+ GM-CSF, TNFa, activated 6 hr	18.94
T cell, TH1 clone HY06, activated	18.99
lung fetal	19.15
T cell, TH1 clone HY06, resting	19.18
T cell, TH1 clone HY06, anergic	19.23
monocytes, LPS, gIFN, IL-10, 4+16 hr	19.3
spleen fetal	19.51
testes fetal	19.7
T cell, TH0 clone Mot 72, resting	19.71
T cell, TH0 clone Mot 72, resting	19.84
DC CD1a+ CD86+, ex CD34+ GM-CSF, TNFa, activated 1+6 hr	19.94
peripheral blood mononuclear cells, activated	20.01
hematopoietic precursor line TF1, activated	20.07
lung fibroblast sarcoma line MRC5, activated	20.18
Splenocytes, activated	20.21
T cell gd clones, resting	20.27
ovary fetal	20.45
T cells CD4+, TH2 polarized, activated	20.57
Splenocytes, resting	20.6
uterus fetal	20.62
DC 95% CD1a+, ex CD34+ GM-CSF, TNFa, activated 1+6 hr	20.94
epithelial cells, unstimulated	20.96
peripheral blood mononuclear cells, resting	20.97
adipose tissue fetal	21.13



B cell line JY, activated	21.28
monocytes, LPS, gIFN, IL-10	21.37
placenta 28 wk	21.38
NK 20 clones pooled, activated	21.55
pool of two normal human lung samples	21.63
normal human thyroid	21.65
epithelial cells, IL-1b activated	21.72
normal human skin	21.84
T cell, TH0 clone Mot 72, anergic	21.87
small intestine fetal	22.01
CD28- T cell clone in pME	22.08
T cell, TH2 clone HY935, activated	22.09
T cell clones, pooled, resting	22.29
Hashimoto's thyroiditis thyroid sample	22.3
NK 20 clones pooled, resting	22.4
B cell EBV lines, resting	22.45
T cell, TH2 clone HY935, resting	22.86
T cell, TH0 clone Mot 72, activated	23.3
monocytes, LPS, gIFN, anti-IL-10, 4+16 hr	23.39
T cell lines Jurkat and Hut78, resting	23.4
T cell, TH0 clone Mot 72, activated	23.56
<i>Pneumocystis carinii</i> pneumonia lung sample	24.05
U937 premonocytic line, resting	25.01
pool of rheumatoid arthritis samples, human	25.85
pool of three heavy smoker human lung samples	26.1
DC 95% CD14+, ex CD34+ GM-CSF, TNFa, activated 1+6 hr	32.69
kidney fetal	33.7
liver fetal	34.4
NK cytotoxic clone, resting	34.49
tonsil inflamed	35.02
normal w.t. monkey lung	35.45
gallbladder fetal	35.84
TR1 T cell clone	35.86
allergic lung sample	36.39
Psoriasis patient skin sample	36.44
normal human colon	37.34
brain fetal	37.35
<i>Ascaris</i> -challenged monkey lung, 4 hr.	37.75
<i>Ascaris</i> -challenged monkey lung, 24 hr.	40
heart fetal	40
normal w.t. monkey colon	40
ulcerative colitis human colon sample	40

Primers specific for DCRS6\_H were designed and used in Taqman quantitative PCR against various human libraries. DCRS6\_H is expressed in innate immune myeloid cells including dendritic cells and monocytes. Expression is also detected in T-cell libraries. These data demonstrate the receptor is expressed in immune cell types and may be regulated by activation conditions.

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**Table for DCRS6\_H**

<b>library description</b>	<b>CT for DCRS6_H</b>
T cell, TH0 clone Mot 72, resting	15.54
T cell, TH0 clone Mot 72, resting	15.7
DC ex monocytes GM-CSF, IL-4, resting	17.84
DC ex monocytes GM-CSF, IL-4, resting	18.19
DC ex monocytes GM-CSF, IL-4, LPS activated 4+16 hr	18.3
DC ex monocytes GM-CSF, IL-4, monokine activated 4+16 hr	18.3
T cell, TH1 clone HY06, resting	18.43
NK cytotoxic clone, resting	18.53
T cell clones, pooled, resting	18.8
T cell, TH1 clone HY06, activated	19.03
T cell, TH2 clone HY935, activated	19.1
TR1 T cell clone	19.12
T cells CD4+, TH2 polarized, activated	20.06
B cell EBV lines, resting	20.3
T cell, TH2 clone HY935, resting	20.48
kidney epithelial carcinoma cell line CHA, activated	21.07
T cell, TH1 clone HY06, anergic	21.14
normal human colon	21.29
NK 20 clones pooled, resting	21.49
T cell gd clones, resting	21.58
gallbladder fetal	22.21
kidney fetal	22.79
liver fetal	22.8
<i>Pneumocystis carinii</i> pneumonia lung sample	23.06
CD28- T cell clone in pME	23.18
T cell, TH0 clone Mot 72, anergic	23.2
ovary fetal	23.51
normal human thyroid	24.03
small intestine fetal	24.13
testes fetal	24.82
epithelial cells, IL-1b activated	26.08
pool of three heavy smoker human lung samples	26.49
placenta 28 wk	26.56
normal w.t. monkey lung	28.65
peripheral blood mononuclear cells,	33.39

activated	
<i>Ascaris</i> -challenged monkey lung, 4 hr.	36.59
spleen fetal	38.43
peripheral blood mononuclear cells, resting	40
T cell, TH0 clone Mot 72, activated	40
T cell lines Jurkat and Hut78, resting	40
Splenocytes, resting	40
Splenocytes, activated	40
B cell line JY, activated	40
NK 20 clones pooled, activated	40
hematopoietic precursor line TF1, activated	40
U937 premonocytic line, resting	40
U937 premonocytic line, activated	40
monocytes, LPS, gIFN, anti-IL-10	40
monocytes, LPS, gIFN, IL-10	40
monocytes, LPS, gIFN, anti-IL-10, 4+16 hr	40
monocytes, LPS, gIFN, IL-10, 4+16 hr	40
monocytes, LPS, 1 hr	40
monocytes, LPS, 6 hr	40
DC 70% CD1a+, ex CD34+ GM-CSF, TNFa, resting	40
DC 70% CD1a+, ex CD34+ GM-CSF, TNFa, activated 1 hr	40
DC 70% CD1a+, ex CD34+ GM-CSF, TNFa, activated 6 hr	40
DC 95% CD1a+, ex CD34+ GM-CSF, TNFa, activated 1+6 hr	40
DC 95% CD14+, ex CD34+ GM-CSF, TNFa, activated 1+6 hr	40
DC CD1a+ CD86+, ex CD34+ GM-CSF, TNFa, activated 1+6 hr	40
epithelial cells, unstimulated	40
lung fibroblast sarcoma line MRC5, activated	40
<i>Ascaris</i> -challenged monkey lung, 24 hr.	40
pool of two normal human lung samples	40
allergic lung sample	40
normal w.t. monkey colon	40
ulcerative colitis human colon sample	40
Hashimoto's thyroiditis thyroid sample	40
pool of rheumatoid arthritis samples, human	40
normal human skin	40
Psoriasis patient skin sample	40
tonsil inflamed	40
lung fetal	40
heart fetal	40
brain fetal	40
adipose tissue fetal	40
uterus fetal	40

T cell, TH0 clone Mot 72, activated

40

- 5 Primers specific for DCRS7\_H were designed and used in Taqman quantitative PCR against various human libraries. DCRS7\_H is expressed in innate immune myeloid cells including dendritic cells and monocytes. Expression is also detected in fetal libraries. These data demonstrate the receptor is expressed in immune cell types and may be regulated by activation conditions.

**Table for DCRS7\_H  
library description**

**CT for  
DCRS7\_H**

fetal uterus	19.05
DC mix	19.34
fetal small intestine	19.46
fetal ovary	19.68
fetal testes	19.75
fetal lung	20.04
CHA	20.24
normal thyroid	20.32
DC/GM/IL-4	20.52
fetal spleen	20.86
normal lung	20.94
TF1	21
allergic lung #19	21.02
Psoriasis skin	21.07
fetal liver	21.15
MRC5	21.15
24 hr. Ascaris lung	21.17
hi dose IL-4 lung	21.23
CD1a+ 95%	21.32
Hashimotos thyroiditis	21.35
Crohns colon 4003197A	21.35
normal lung pool	21.36
70% DC resting	21.42
fetal kidney	21.58
adult placenta	21.68
lung 121897-1	21.8
Pneumocystis carinii lung	21.81
#20	
A549 unstim.	21.89
normal colon #22	21.94
18 hr. Ascaris lung	22.09
normal skin	22.1
Crohns colon 9609C144	22.13
fetal adipose tissue	22.35
D6	22.39

DC resting CD34-derived	22.45
DC TNF/TGFb act CD34-der.	22.54
fetal brain	22.9
DC CD40L activ. mono-deriv.	22.91
Crohns colon 403242A	22.91
ulcerative colitis colon #26	23
RA synovium pool	23.06
A549 activated	23.06
mono + IL-10	23.42
DC LPS	23.49
Mot 72 activated	23.66
CD1a+ CD86+	23.86
HY06 resting	23.87
U937 activated	23.97
inflammed tonsil	23.97
D1	24.06
M1	24.17
CD14+ 95%	24.21
lung 080698-2	24.28
4 hr. Ascaris lung	24.37
Jurkat activated pSPORT	24.42
DC resting mono-derived	24.48
HY06 activated	24.54
C+	24.64
Splenocytes resting	24.65
U937/CD004 resting	24.96
PBMC resting	25.8
Mot 72 resting	25.91
mono + anti-IL-10	26.14
NK pool	26.99
HY06 anti-peptide	27.34
mast cell pME	27.38
Tc gamma delta	28.14
TC1080 CD28- pMET7	31.05
PBMC activated	31.89
NK non cytotox.	32.3
RV-C30 TR1 pMET7	32.5
Bc	33.72
C-	33.8
Splenocytes activated	34.7
JY	35.05
NK cytotox.	36.44
NKL/IL-2	37.59
HY935 resting	37.6
NK pool activated	38.15
Mot 72 anti-peptide	38.87
fetal heart	40.92

B21 resting	42.05
Jurkat resting pSPORT	42.8
B21 activated	43.09
NKA6 pSPORT	44.85
HY935 activated	45
M6	45

5 Primers specific for DCRS9\_H were designed and used in Taqman quantitative PCR against various human libraries. DCRS9\_H is expressed T-cells, fetal lung, and resting monocytes. These data demonstrate the receptor is expressed in immune cell types and may be regulated by activation conditions.

**Table for DCRS9\_H  
library description CT for  
DCRS9\_H**

HY06 resting	22.35
fetal lung	22.63
HY06 anti-peptide	22.72
HY06 activated	22.96
U937/CD004 resting	24.16
fetal small intestine	24.94
JY	25.04
Mot 72 resting	25.12
Jurkat activated pSPORT	25.2
RV-C30 TR1 pMET7	26.51
fetal kidney	26.76
MRC5	27.2
Psoriasis skin	27.3
Tc gamma delta	27.37
Crohns colon 4003197A	27.44
fetal spleen	27.72
normal lung	27.83
Hashimotos thyroiditis	28.03
B21 resting	28.32
TF1	28.39
NK cytotox.	28.44
TC1080 CD28- pMET7	28.61
Pneumocystis carinii lung #20	29.05
U937 activated	29.06
HY935 resting	29.09
CD1a+ 95%	29.13

B21 activated	29.2
Mot 72 activated	29.21
fetal testes	29.27
lung 080698-2	29.32
Jurkat resting	29.38
pSPORT	
CD14+ 95%	29.38
normal thyroid	29.53
Mot 72 anti-peptide	29.65
Splenocytes resting	29.85
Crohns colon	30.28
9609C144	
lung 121897-1	30.37
24 hr. Ascaris lung	30.59
hi dose IL-4 lung	30.8
CD1a+ CD86+	31.42
normal skin	31.73
fetal uterus	31.79
PBMC activated	31.82
inflammed tonsil	31.98
fetal brain	32.21
RA synovium pool	32.77
allergic lung #19	33.18
18 hr. Ascaris lung	33.42
adult placenta	33.43
normal lung pool	33.45
Crohns colon	33.52
403242A	
NK pool	33.72
HY935 activated	33.75
DC/GM/IL-4	34.28
DC resting mono-derived	34.57
fetal ovary	35.06
fetal adipose tissue	35.07
CHA	35.2
PBMC resting	35.95
Bc	36.19
A549 unstim.	36.4
fetal heart	36.87
ulcerative colitis colon #26	37.83
C-	38.32
4 hr. Ascaris lung	40.2
D6	40.62
C+	44.38

A549 activated	44.58
Splenocytes	45
activated	
NK pool activated	45
NKA6 pSPORT	45
NKL/IL-2	45
NK non cytotox.	45
mono + anti-IL-10	45
mono + IL-10	45
M1	45
M6	45
70% DC resting	45
D1	45
DC LPS	45
DC mix	45
fetal liver	45
mast cell pME	45
DC CD40L activ.	45
mono-deriv.	
DC resting CD34- derived	45
DC TNF/TGFb act	45
CD34-der.	
normal colon #22	45



## V. Cloning of species counterparts

Various strategies are used to obtain species counterparts of the DCRSs, preferably from other primates or rodents. One method is by cross hybridization using closely related species DNA probes. It may be useful to go into evolutionarily similar species as intermediate steps. Another method is by using specific PCR primers based on the identification of blocks of similarity or difference between genes, e.g., areas of highly conserved or nonconserved polypeptide or nucleotide sequence. Sequence database searches may identify species counterparts.

## 10 VI. Production of mammalian protein

An appropriate, e.g., GST, fusion construct is engineered for expression, e.g., in *E. coli*. For example, a mouse IGIF pGex plasmid is constructed and transformed into *E. coli*. Freshly transformed cells are grown, e.g., in LB medium containing 50 µg/ml ampicillin and induced with IPTG (Sigma, St. Louis, MO). After overnight induction, the bacteria are harvested and the pellets containing the appropriate protein are isolated. The pellets are homogenized, e.g., in TE buffer (50 mM Tris-base pH 8.0, 10 mM EDTA and 2 mM pefabloc) in 2 liters. This material is passed through a microfluidizer (Microfluidics, Newton, MA) three times. The fluidized supernatant is spun down on a Sorvall GS-3 rotor for 1 h at 13,000 rpm. The resulting supernatant containing the cytokine receptor protein is filtered and passed over a glutathione-SEPHAROSE column equilibrated in 50 mM Tris-base pH 8.0. Fractions containing the DCRS8-GST fusion protein are pooled and cleaved, e.g., with thrombin (Enzyme Research Laboratories, Inc., South Bend, IN). The cleaved pool is then passed over a Q-SEPHAROSE column equilibrated in 50 mM Tris-base. Fractions containing DCRS8 are pooled and diluted in cold distilled H<sub>2</sub>O, to lower the conductivity, and passed back over a fresh Q-Sepharose column, alone or in succession with an immunoaffinity antibody column. Fractions containing the DCRS8 protein are pooled, aliquoted, and stored in the -70° C freezer.

Comparison of the CD spectrum with cytokine receptor protein may suggest that the protein is correctly folded. See Hazuda, et al. (1969) J. Biol. Chem. 264:1689-1693.

## 30 VII. Preparation of specific antibodies

Inbred Balb/c mice are immunized intraperitoneally with recombinant forms of the protein, e.g., purified DCRS8 or stable transfected NIH-3T3 cells. Animals are boosted at appropriate time points with protein, with or without additional adjuvant, to further stimulate antibody production. Serum is collected, or hybridomas produced with harvested spleens.

Alternatively, Balb/c mice are immunized with cells transformed with the gene or fragments thereof, either endogenous or exogenous cells, or with isolated membranes enriched for expression of the antigen. Serum is collected at the appropriate time, typically after numerous further administrations. Various gene therapy techniques may be useful, e.g., in producing protein in situ, for generating an immune response. Serum or antibody preparations may be cross-absorbed or immunoselected to prepare substantially purified antibodies of defined specificity and high affinity.

Monoclonal antibodies may be made. For example, splenocytes are fused with an appropriate fusion partner and hybridomas are selected in growth medium by standard procedures. Hybridoma supernatants are screened for the presence of antibodies which bind to the DCRS8, e.g., by ELISA or other assay. Antibodies which specifically recognize specific DCRS8 embodiments may also be selected or prepared.

In another method, synthetic peptides or purified protein are presented to an immune system to generate monoclonal or polyclonal antibodies. See, e.g., Coligan (ed. 1991) Current Protocols in Immunology Wiley/Greene; and Harlow and Lane (1989) Antibodies: A Laboratory Manual Cold Spring Harbor Press. In appropriate situations, the binding reagent is either labeled as described above, e.g., fluorescence or otherwise, or immobilized to a substrate for panning methods. Nucleic acids may also be introduced into cells in an animal to produce the antigen, which serves to elicit an immune response. See, e.g., Wang, et al. (1993) Proc. Nat'l. Acad. Sci. 90:4156-4160; Barry, et al. (1994) BioTechniques 16:616-619; and Xiang, et al. (1995) Immunity 2: 129-135.

#### VIII. Production of fusion proteins

Various fusion constructs are made with DCRS8 or DCRS9. A portion of the appropriate gene is fused to an epitope tag, e.g., a FLAG tag, or to a two hybrid system construct. See, e.g., Fields and Song (1989) Nature 340:245-246.

The epitope tag may be used in an expression cloning procedure with detection with anti-FLAG antibodies to detect a binding partner, e.g., ligand for the respective cytokine receptor. The two hybrid system may also be used to isolate proteins which specifically bind to the receptor subunit.

#### IX. Structure activity relationship

Information on the criticality of particular residues is determined using standard procedures and analysis. Standard mutagenesis analysis is performed, e.g., by generating many different variants at determined positions, e.g., at the positions identified above, and evaluating biological activities of the variants. This may be performed to the extent of determining positions which modify activity, or to focus on specific positions to

determine the residues which can be substituted to either retain, block, or modulate biological activity.

Alternatively, analysis of natural variants can indicate what positions tolerate natural mutations. This may result from populational analysis of variation among individuals, or across strains or species. Samples from selected individuals are analyzed, e.g., by PCR analysis and sequencing. This allows evaluation of population polymorphisms.

#### X. Isolation of a ligand

A cytokine receptor can be used as a specific binding reagent to identify its binding partner, by taking advantage of its specificity of binding, much like an antibody would be used. The binding receptor may be a heterodimer of receptor subunits; or may involve, e.g., a complex of the DCRS8 with another cytokine receptor subunit. A binding reagent is either labeled as described above, e.g., fluorescence or otherwise, or immobilized to a substrate for panning methods.

The binding composition is used to screen an expression library made from a cell line which expresses a binding partner, i.e., ligand, preferably membrane associated. Standard staining techniques are used to detect or sort surface expressed ligand, or surface expressing transformed cells are screened by panning. Screening of intracellular expression is performed by various staining or immunofluorescence procedures. See also McMahan, et al. (1991) EMBO J. 10:2821-2832.

For example, on day 0, precoat 2-chamber permanox slides with 1 ml per chamber of fibronectin, 10 ng/ml in PBS, for 30 min at room temperature. Rinse once with PBS. Then plate COS cells at  $2-3 \times 10^5$  cells per chamber in 1.5 ml of growth media. Incubate overnight at 37 C.

On day 1 for each sample, prepare 0.5 ml of a solution of 66  $\mu$ g/ml DEAE-dextran, 66  $\mu$ M chloroquine, and 4  $\mu$ g DNA in serum free DME. For each set, a positive control is prepared, e.g., of DCRS8-FLAG cDNA at 1 and 1/200 dilution, and a negative mock. Rinse cells with serum free DME. Add the DNA solution and incubate 5 hr at 37 C. Remove the medium and add 0.5 ml 10% DMSO in DME for 2.5 min. Remove and wash once with DME. Add 1.5 ml growth medium and incubate overnight.

On day 2, change the medium. On days 3 or 4, the cells are fixed and stained. Rinse the cells twice with Hank's Buffered Saline Solution (HBSS) and fix in 4% paraformaldehyde (PFA)/glucose for 5 min. Wash 3X with HBSS. The slides may be stored at -80 C after all liquid is removed. For each chamber, 0.5 ml incubations are performed as follows. Add HBSS/saponin (0.1%) with 32  $\mu$ l/ml of 1 M  $\text{NaN}_3$  for 20 min. Cells are then washed with HBSS/saponin 1X. Add appropriate DCRS8 or

DCRS8/antibody complex to cells and incubate for 30 min. Wash cells twice with HBSS/saponin. If appropriate, add first antibody for 30 min. Add second antibody, e.g., Vector anti-mouse antibody, at 1/200 dilution, and incubate for 30 min. Prepare ELISA solution, e.g., Vector Elite ABC horseradish peroxidase solution, and preincubate for 30 min. Use, e.g., 1 drop of solution A (avidin) and 1 drop solution B (biotin) per 2.5 ml HBSS/saponin. Wash cells twice with HBSS/saponin. Add ABC HRP solution and incubate for 30 min. Wash cells twice with HBSS, second wash for 2 min, which closes cells. Then add Vector diaminobenzoic acid (DAB) for 5 to 10 min. Use 2 drops of buffer plus 4 drops DAB plus 2 drops of H<sub>2</sub>O<sub>2</sub> per 5 ml of glass distilled water.

Carefully remove chamber and rinse slide in water. Air dry for a few minutes, then add 1 drop of Crystal Mount and a cover slip. Bake for 5 min at 85-90 C.

Evaluate positive staining of pools and progressively subclone to isolation of single genes responsible for the binding.

Alternatively, receptor reagents are used to affinity purify or sort out cells expressing a putative ligand. See, e.g., Sambrook, et al. or Ausubel, et al.

Another strategy is to screen for a membrane bound receptor by panning. The receptor cDNA is constructed as described above. Immobilization may be achieved by use of appropriate antibodies which recognize, e.g., a FLAG sequence of a DCRS8 fusion construct, or by use of antibodies raised against the first antibodies. Recursive cycles of selection and amplification lead to enrichment of appropriate clones and eventual isolation of receptor expressing clones.

Phage expression libraries can be screened by mammalian DCRS8. Appropriate label techniques, e.g., anti-FLAG antibodies, will allow specific labeling of appropriate clones.

We tested the ability of DCRS receptors to specifically bind IL-17 family cytokines. Recombinant FLAG-hIL-17 family cytokines were used in binding experiments on Baf/3 DCRS receptor transfected expressing recombinant IL-17R\_H, DCRS6\_H, DCRS7\_H, DCRS8\_H and DCRS9\_H and analyzed by FACS. We can demonstrate specific binding of IL-17 family member IL-74 to DCRS6 expressing Baf/3 cells. In additional experiments we have shown IL-17 specific binding to IL-17R\_H, DCRS7\_H, DCRS8\_H. Further experiments show IL-71 binding to DCRS8\_Hu transfectants. These experiments demonstrate the sequence homology among IL-17 related cytokine receptors confers functional binding to IL-17 cytokines.

All citations herein are incorporated herein by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

Many modifications and variations of this invention can be made without departing from its spirit and scope, as will be apparent to those skilled in the art. The specific embodiments described herein are offered by way of example only, and the invention is to be limited by the terms of the appended claims, along with the full scope  
5 of equivalents to which such claims are entitled; and the invention is not to be limited by the specific embodiments that have been presented herein by way of example.

## WHAT IS CLAIMED IS:

1. A composition of matter selected from:
  - a) a substantially pure or recombinant polypeptide comprising at least three distinct nonoverlapping segments of at least four amino acids identical to segments of SEQ ID NO: 14;
  - b) a substantially pure or recombinant polypeptide comprising at least two distinct nonoverlapping segments of at least five amino acids identical to segments of SEQ ID NO: 14;
  - c) a natural sequence DCRS8 comprising mature SEQ ID NO: 14;
  - d) a fusion polypeptide comprising DCRS8 sequence;
  - e) a substantially pure or recombinant polypeptide comprising at least three distinct nonoverlapping segments of at least four amino acids identical to segments of SEQ ID NO: 17 or 20;
  - f) a substantially pure or recombinant polypeptide comprising at least two distinct nonoverlapping segments of at least five amino acids identical to segments of SEQ ID NO: 17 or 20;
  - g) a natural sequence DCRS9 comprising mature SEQ ID NO: 17 or 20; or
  - h) a fusion polypeptide comprising DCRS9 sequence.
2. The substantially pure or isolated antigenic polypeptide of Claim 1, wherein said distinct nonoverlapping segments of identity include:
  - a) one of at least eight amino acids;
  - b) one of at least four amino acids and a second of at least five amino acids;
  - c) at least three segments of at least four, five, and six amino acids, or
  - d) one of at least twelve amino acids.
3. The composition of matter of Claim 1, wherein said:
  - a) polypeptide:
    - i) comprises a mature sequence of Table 3 or 4;
    - ii) is an unglycosylated form of DCRS8 or DCRS9;
    - iii) is from a primate, such as a human;
    - iv) comprises at least seventeen amino acids of SEQ ID NO: 14 or 17;
    - v) exhibits at least four nonoverlapping segments of at least seven amino acids of SEQ ID NO: 14 or 17;
    - vi) is a natural allelic variant of DCRS8 or DCRS9;
    - vii) has a length at least about 30 amino acids;

viii) exhibits at least two non-overlapping epitopes which are specific for a primate DCRS8 or DCRS9;

ix) is glycosylated;

x) has a molecular weight of at least 30 kD with natural glycosylation;

5 xi) is a synthetic polypeptide;

xii) is attached to a solid substrate;

xiii) is conjugated to another chemical moiety;

xiv) is a 5-fold or less substitution from natural sequence; or

xv) is a deletion or insertion variant from a natural sequence.

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4. A composition comprising:

a) a substantially pure DCRS8 or DCRS9 and another cytokine receptor family member;

b) a sterile DCRS8 or DCRS9 polypeptide of Claim 1;

15 c) said DCRS8 or DCRS9 polypeptide of Claim 1 and a carrier, wherein said carrier is:

i) an aqueous compound, including water, saline, and/or buffer; and/or

ii) formulated for oral, rectal, nasal, topical, or parenteral administration.

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5. The fusion polypeptide of Claim 1, comprising:

a) mature protein sequence of Table 3 or 4;

b) a detection or purification tag, including a FLAG, His6, or Ig sequence; or

c) sequence of another cytokine receptor protein.

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6. A kit comprising a polypeptide of Claim 1, and:

a) a compartment comprising said protein or polypeptide; or

b) instructions for use or disposal of reagents in said kit.

7. A binding compound comprising an antigen binding site from an antibody, which specifically binds to a natural DCRS8 or DCRS9 polypeptide of Claim 1, wherein:

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a) said binding compound is in a container;

b) said DCRS8 or DCRS9 polypeptide is from a human;

c) said binding compound is an Fv, Fab, or Fab2 fragment;

d) said binding compound is conjugated to another chemical moiety; or

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e) said antibody:

i) is raised against a peptide sequence of a mature polypeptide of Table 3 or 4;

- ii) is raised against a mature DCRS8 or DCRS9;
- iii) is raised to a purified human DCRS8 or DCRS9;
- iv) is immunoselected;
- v) is a polyclonal antibody;
- vi) binds to a denatured DCRS8 or DCRS9;
- vii) exhibits a  $K_d$  to antigen of at least 30  $\mu\text{M}$ ;
- viii) is attached to a solid substrate, including a bead or plastic membrane;
- ix) is in a sterile composition; or
- x) is detectably labeled, including a radioactive or fluorescent label.

8. A kit comprising said binding compound of Claim 7, and:

- a) a compartment comprising said binding compound; or
- b) instructions for use or disposal of reagents in said kit.

9. A method of producing an antigen:antibody complex, comprising contacting under appropriate conditions a primate DCRS8 or DCRS9 polypeptide with an antibody of Claim 7, thereby allowing said complex to form.

10. The method of Claim 9, wherein:

- a) said complex is purified from other cytokine receptors;
- b) said complex is purified from other antibody;
- c) said contacting is with a sample comprising an interferon;
- d) said contacting allows quantitative detection of said antigen;
- e) said contacting is with a sample comprising said antibody; or
- f) said contacting allows quantitative detection of said antibody.

11. A composition comprising:

- a) a sterile binding compound of Claim 7, or
- b) said binding compound of Claim 7 and a carrier, wherein said carrier is:
  - i) an aqueous compound, including water, saline, and/or buffer; and/or
  - ii) formulated for oral, rectal, nasal, topical, or parenteral administration.

12. An isolated or recombinant nucleic acid encoding said polypeptide of Claim 1, wherein said:

- a) DCRS8 or DCRS9 is from a human; or
- b) said nucleic acid:
  - i) encodes an antigenic peptide sequence of Table 3 or 4;



- ii) encodes a plurality of antigenic peptide sequences of Table 3 or 4;
- iii) exhibits identity over at least thirteen nucleotides to a natural cDNA encoding said segment;
- iv) is an expression vector;
- 5 v) further comprises an origin of replication;
- vi) is from a natural source;
- vii) comprises a detectable label;
- viii) comprises synthetic nucleotide sequence;
- ix) is less than 6 kb, preferably less than 3 kb;
- 10 x) is from a primate;
- xi) comprises a natural full length coding sequence;
- xii) is a hybridization probe for a gene encoding said DCRS8 or DCRS9;
- or
- xiii) is a PCR primer, PCR product, or mutagenesis primer.

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13. A cell or tissue comprising said recombinant nucleic acid of Claim 12.

14. The cell of Claim 13, wherein said cell is:

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- a) a prokaryotic cell;
- b) a eukaryotic cell;
- c) a bacterial cell;
- d) a yeast cell;
- e) an insect cell;
- f) a mammalian cell;
- 25 g) a mouse cell;
- h) a primate cell; or
- i) a human cell.

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15. A kit comprising said nucleic acid of Claim 12, and:

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- a) a compartment comprising said nucleic acid;
- b) a compartment further comprising a primate DCRS8 or DCRS9 polypeptide;
- or
- c) instructions for use or disposal of reagents in said kit.

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16. A nucleic acid which:

- a) hybridizes under wash conditions of 30 minutes at 30° C and less than 2M salt to the coding portion of SEQ ID NO: 13 or 16; or

- b) exhibits identity over a stretch of at least about 30 nucleotides to a primate DCRS8 or DCRS9.

17. The nucleic acid of Claim 16, wherein:

- a) said wash conditions are at 45° C and/or 500 mM salt; or
- b) said stretch is at least 55 nucleotides.

18. The nucleic acid of Claim 16, wherein:

- a) said wash conditions are at 55° C and/or 150 mM salt; or
- b) said stretch is at least 75 nucleotides.

19. A method of modulating physiology or development of a cell or tissue culture cells comprising contacting said cell with an agonist or antagonist of a mammalian DCRS8 or DCRS9.

20. The method of Claim 19, wherein said cell is transformed with a nucleic acid encoding said DCRS8 or DCRS9 and another cytokine receptor subunit.

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DDCRS7_Mu      RTALLHSADG-AGYERLVGALASALSQMP--LRVAVDLWSRRE-LSAHGALAWFHHQR
DDCRS7_Hu      RAALLYSADD-SGFERLVGALASALCQLP--LRVAVDLWSRRE-LSAQGPVAFWHAQR
IIL-17R_Hu     RKVWIYSADH-PLYVDVVLKFAQFLLTACG--TEVALDLL EEQA-ISEAGVMTWVGRQK
IIL-17R_Mu     RKVWIVYSADH-PLYVEVVLKFAQFLITACG--TEVALDLL EEQV-ISEVGVMTWVSRQK
DDCRS10        RKVFITYSMD---TAMEVVKFVNFLLVNG--FQTAIDIFEDR--IRGIDI IKWMERYL
DDCRS10_Mu     RKVFITYSMD---TAMEVVKFVNFLLVNG--FQTAIDIFEDR--IRGIDI IKWMERYL
DDCRS9_Hu      RPYLLHAAADS-EAQRRLVGALAE LLRAALGGGRDVI VDLWEGRH-VARVGPLPWLWAAR
DDCRS8_Hu      PKVFCLYSSKDGQNHMNVVQCFAYFLQDFCG--CEVALDLWEDFS-LCREGQREWVIQKI
IIL-17R_Ce     VKVMI VYADDN-DLHTDCVKKKLVENLRNCAS--CDPVFDLEKLI--TAEI VPSRWLVDQI
DDCRS6_Hu      IKVLVVPSEI--CFHHTICYFTEFLQNHCR--SEVILEKWQKKK-IAEMGPVQWLATQK
DDCRS6_Ce      FKVMLVCPEVS-GRDEDFMMRIADALKKSN---NKVVCDRWFEDSKNAEENMLHWVYEQT

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DCRS7_Mu      RRILQEGGVILLFSPAAVAQCQ---QWLQLQTVEP---GP---HDALAAWLSCVLPDFL
DCRS7_Hu      RQTLQEGGVVLLFSPGAVALCS---EWLQDGVSGPGAHP---HDAFRASLSCVLPDFL
IL-17R_Hu     QEMVESNSKIIIVLCRSGTRAKWQALLGRGAP-VRLRCDHGKPV-GDLFTAAMNMILPDFK
IL-17R_Mu     QEMVESNSKIIILCSRGTQAKWKAILGWAEPVQLRCDHWKPA-GDLFTAAMNMILPDFK
DCRS10        R---DKTVMIIVAISPKYKQDVE---GAESQLDED-EHGL---HTKYIHRM-MQIEFIK
DCRS10_Mu     R---DKTVMIIVAISPKYKQDVE---GAESQLDED-EHGL---HTKYIHRM-MQIEFIS
DCRS9_Hu      TRVAREQGTVLLWSGADLRPVS---GPDPR-RAAP-----LLA---LLHAAP
DCRS8_Hu      H---ESQFIIVVCSKGMKYFVD---KKNYKHKGGRSGK---GELFLVAVSAIAEKLRL
IL-17R_Ce     S---SLKKFIIIVVSDCAEKILD---TEASETHQLVQARP--FADLFGPAMEMIIRDAT
DCRS6_Hu      K---AADKVVFLLSNDVNSVCD---GTCGKSEGSSENS---QDLFPLAFNLFCSDLR
DCRS6_Ce      K---IAEKIIIVFHSAYYHPRCG---IYDVINNFFPCTDPR---LAHIALT---PEAQ

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**FIG. 1A**

DCRS7_Mu	QGRATGR-----YVGVFYFDGLLHPDSVPSPFRVAPLFSLP-SQLPAFLDALQ--GGCSTS
DCRS7_Hu	QGRAPGS-----YVGACFDRLHHPDAVPALFRTVPVFTLP-SQLPDPFLGALQ--QPRAPR
IL-17R_Hu	RPACFGT-----YVVCYFSEVSCDGDVPDLFGAAPRYPLM-DRFEEVYFRIQ--DLEMFO
IL-17R_Mu	RPACFGT-----YVVCYFSGICSERDVPDLFNITSRYPLM-DRFEEVYFRIQ--DLEMFE
DCRS10	QGSMNFR-----FIPVLFPPNAK-KEHVPTWLQNTHVSWP-KNKNILLRLL-REEEYVA
DCRS10_Mu	QGSMNFR-----FIPVLFPPNAK-KEHVPTWLQNTHVSWP-KNKNILLRLL-REEEYVA
DCRS9_Hu	RPL-----LLAYFSRLCAKGDIPPPLRALPRYRL-RDLPRLLRALD--ARPFAE
DCRS8_Hu	QAKQSSSAALSKFIAVYFDYSC-EGDVPGLDLSTKYRLM-DNLPQLCSHLHSRDHGLQE
IL-17R_Ce	HNFPPEAR---KKYAVVRFNYSPP---HVPPNLAILNLPTFIPEQFAQLTAFLHN-VEHTER
DCRS6_Hu	SQIHLHK-----YVVVYFREID-TKDDYNALSVCPKYHLM-KDATAFCAELL---HVKQQ
DCRS6_Ce	RSVPKEV-----EYVLP RDQKLL--EDAFDITIADPLVIDIPIEDVAIPENVP--IHHESC

DCRS7_Mu	AGRPADRVRE-----VT-----QALRSALDSCTS-----
DCRS7_Hu	SGRLQERAEQ-----VS-----RALQPALDSYFHPP-----
IL-17R_Hu	PGRMHRVGE LSGDNYLRS---PGGRQLRAALDRFRDWQVRCPDW
IL-17R_Mu	PGRMHVREL TGDNYLQS---PSGRQLKEAVLRFQEWQTQCPDW
DCRS10	P-----PRGPL-----PTLQVVPL-----
DCRS10_Mu	P-----PRGPL-----PTLQVVPL-----
DCRS9_Hu	ATSWGRLGAR-----QRRQSRLELCSR-----
DCRS8_Hu	PGQHTRQGSR-----RNYFRSKGRSLYVAICNMHQFIDEEDPW
IL-17R_Ce	ANVTQNISEA-----Q-----IHEWNLCASRMMSFFVRNPWN
DCRS6_Hu	VS-----AGKR-----SQACHDGCCSL-----
DCRS6_Ce	DSIDSRNNSK-----THSTD SGVSSLSS-----NS--

FIG. 1B

## SEQUENCE SUBMISSION

SEQ ID NO: 1 is primate DCRS6 nucleotide sequence.  
SEQ ID NO: 2 is primate DCRS6 polypeptide sequence.  
SEQ ID NO: 3 is primate DCRS6 reverse translation.  
SEQ ID NO: 4 is rodent DCRS6 nucleotide sequence.  
SEQ ID NO: 5 is rodent DCRS6 polypeptide sequence.  
SEQ ID NO: 6 is rodent DCRS6 reverse translation.  
SEQ ID NO: 7 is primate DCRS7 nucleotide sequence.  
SEQ ID NO: 8 is primate DCRS7 polypeptide sequence.  
SEQ ID NO: 9 is primate DCRS7 reverse translation.  
SEQ ID NO: 10 is rodent DCRS7 nucleotide sequence.  
SEQ ID NO: 11 is rodent DCRS7 polypeptide sequence.  
SEQ ID NO: 12 is rodent DCRS7 reverse translation.  
SEQ ID NO: 13 is primate DCRS8 nucleotide sequence.  
SEQ ID NO: 14 is primate DCRS8 polypeptide sequence.  
SEQ ID NO: 15 is primate DCRS8 reverse translation.  
SEQ ID NO: 16 is primate DCRS9 nucleotide sequence.  
SEQ ID NO: 17 is primate DCRS9 polypeptide sequence.  
SEQ ID NO: 18 is primate DCRS9 reverse translation.  
SEQ ID NO: 19 is rodent DCRS9 nucleotide sequence.  
SEQ ID NO: 20 is rodent DCRS9 polypeptide sequence.  
SEQ ID NO: 21 is rodent DCRS9 reverse translation.  
SEQ ID NO: 22 is primate DCRS10 nucleotide sequence.  
SEQ ID NO: 23 is primate DCRS10 polypeptide sequence.  
SEQ ID NO: 24 is primate DCRS10 reverse translation.  
SEQ ID NO: 25 is rodent DCRS10 nucleotide sequence.  
SEQ ID NO: 26 is rodent DCRS10 polypeptide sequence.  
SEQ ID NO: 27 is rodent DCRS10 reverse translation.  
SEQ ID NO: 28 is primate IL-17 receptor peptide sequence.  
SEQ ID NO: 29 is rodent IL-17 receptor peptide sequence.  
SEQ ID NO: 30 is worm IL-17 receptor peptide sequence.  
SEQ ID NO: 31 is worm DCRS6 nucleotide sequence.

<110> Schering Corporation

<120> Mammalian Receptor Proteins; Related Reagents and  
Methods

<130> DX01170K PCT

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<150> US 60/206,862

<151> 2000-05-24

<160> 31

<170> PatentIn Ver. 2.0

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Homo sapiens

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                    -10                      -5                -1  1

gta ccc cga gag ccg acc gtt caa tgt ggc tct gaa act ggg cca tct      96
Val Pro Arg Glu Pro Thr Val Gln Cys Gly Ser Glu Thr Gly Pro Ser
                    5                      10                15

cca gag tgg atg cta caa cat gat cta atc ccg gga gac ttg agg gac      144
Pro Glu Trp Met Leu Gln His Asp Leu Ile Pro Gly Asp Leu Arg Asp
                    20                      25                30

ctc cga gta gaa cct gtt aca act agt gtt gca aca ggg gac tat tca      192
Leu Arg Val Glu Pro Val Thr Thr Ser Val Ala Thr Gly Asp Tyr Ser
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att ttg atg aat gta agc tgg gta ctc cgg gca gat gcc agc atc cgc      240
Ile Leu Met Asn Val Ser Trp Val Leu Arg Ala Asp Ala Ser Ile Arg
                    50                      55                60                65

ttg ttg aag gcc acc aag att tgt gtg acg ggc aaa agc aac ttc cag      288
Leu Leu Lys Ala Thr Lys Ile Cys Val Thr Gly Lys Ser Asn Phe Gln
                    70                      75                80

tcc tac agc tgt gtg agg tgc aat tac aca gag gcc ttc cag act cag      336
Ser Tyr Ser Cys Val Arg Cys Asn Tyr Thr Glu Ala Phe Gln Thr Gln
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acc aga ccc tct ggt ggt aaa tgg aca ttt tcc tat atc ggc ttc cct      384
Thr Arg Pro Ser Gly Gly Lys Trp Thr Phe Ser Tyr Ile Gly Phe Pro
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gta gag ctg aac aca gtc tat ttc att ggg gcc cat aat att cct aat      432
Val Glu Leu Asn Thr Val Tyr Phe Ile Gly Ala His Asn Ile Pro Asn
                    115                     120                125

gca aat atg aat gaa gat ggc cct tcc atg tct gtg aat ttc acc tca      480
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cca ggc tgc cta gac cac ata atg aaa tat aaa aaa aag tgt gtc aag      528
Pro Gly Cys Leu Asp His Ile Met Lys Tyr Lys Lys Lys Cys Val Lys
                    150                     155                160

gcc gga agc ctg tgg gat ccg aac atc act gct tgt aag aag aat gag      576
Ala Gly Ser Leu Trp Asp Pro Asn Ile Thr Ala Cys Lys Lys Asn Glu
                    165                     170                175

gag aca gta gaa gtg aac ttc aca acc act ccc ctg gga aac aga tac      624
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Glu Pro His Gln Lys Lys Gln Thr Arg Ala Ser Val Val Ile Pro Val	
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Thr Gly Asp Ser Glu Gly Ala Thr Val Gln Leu Thr Pro Tyr Phe Pro	
230 235 240	
act tgt ggc agc gac tgc atc cga cat aaa gga aca gtt gtg ctc tgc	816
Thr Cys Gly Ser Asp Cys Ile Arg His Lys Gly Thr Val Val Leu Cys	
245 250 255	
cca caa aca ggc gtc cct ttc cct ctg gat aac aac aaa agc aag ccg	864
Pro Gln Thr Gly Val Pro Phe Pro Leu Asp Asn Asn Lys Ser Lys Pro	
260 265 270	
gga ggc tgg ctg cct ctc ctc ctg ctg tct ctg ctg gtg gcc aca tgg	912
Gly Gly Trp Leu Pro Leu Leu Leu Ser Leu Leu Val Ala Thr Trp	
275 280 285	
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Val Leu Val Ala Gly Ile Tyr Leu Met Trp Arg His Glu Arg Ile Lys	
290 295 300 305	
aag act tcc ttt tct acc acc aca cta ctg ccc ccc att aag gtt ctt	1008
Lys Thr Ser Phe Ser Thr Thr Thr Leu Leu Pro Pro Ile Lys Val Leu	
310 315 320	
gtg gtt tac cca tct gaa ata tgt ttc cat cac aca att tgt tac ttc	1056
Val Val Tyr Pro Ser Glu Ile Cys Phe His His Thr Ile Cys Tyr Phe	
325 330 335	
act gaa ttt ctt caa aac cat tgc aga agt gag gtc atc ctt gaa aag	1104
Thr Glu Phe Leu Gln Asn His Cys Arg Ser Glu Val Ile Leu Glu Lys	
340 345 350	
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Trp Gln Lys Lys Lys Ile Ala Glu Met Gly Pro Val Gln Trp Leu Ala	
355 360 365	
act caa aag aag gca gca gac aaa gtc gtc ttc ctt ctt tcc aat gac	1200
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gtc aac agt gtg tgc gat ggt acc tgt ggc aag agc gag ggc agt ccc	1248
Val Asn Ser Val Cys Asp Gly Thr Cys Gly Lys Ser Glu Gly Ser Pro	
390 395 400	
agt gag aac tct caa gac ctc ttc ccc ctt gcc ttt aac ctt ttc tgc	1296
Ser Glu Asn Ser Gln Asp Leu Phe Pro Leu Ala Phe Asn Leu Phe Cys	
405 410 415	
agt gat cta aga agc cag att cat ctg cac aaa tac gtg gtg gtc tac	1344
Ser Asp Leu Arg Ser Gln Ile His Leu His Lys Tyr Val Val Val Tyr	
420 425 430	

ttt aga gag att gat aca aaa gac gat tac aat gct ctc agt gtc tgc 1392  
 Phe Arg Glu Ile Asp Thr Lys Asp Asp Tyr Asn Ala Leu Ser Val Cys  
 435 440 445  
 ccc aag tac cac ctc atg aag gat gcc act gct ttc tgt gca gaa ctt 1440  
 Pro Lys Tyr His Leu Met Lys Asp Ala Thr Ala Phe Cys Ala Glu Leu  
 450 455 460 465  
 ctc cat gtc aag cag cag gtg tca gca gga aaa aga tca caa gcc tgc 1488  
 Leu His Val Lys Gln Gln Val Ser Ala Gly Lys Arg Ser Gln Ala Cys  
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 His Asp Gly Cys Ser Leu  
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 Arg Val Glu Pro Val Thr Thr Ser Val Ala Thr Gly Asp Tyr Ser Ile  
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 55 60 65  
 Leu Lys Ala Thr Lys Ile Cys Val Thr Gly Lys Ser Asn Phe Gln Ser  
 70 75 80  
 Tyr Ser Cys Val Arg Cys Asn Tyr Thr Glu Ala Phe Gln Thr Gln Thr  
 85 90 95  
 Arg Pro Ser Gly Gly Lys Trp Thr Phe Ser Tyr Ile Gly Phe Pro Val  
 100 105 110  
 Glu Leu Asn Thr Val Tyr Phe Ile Gly Ala His Asn Ile Pro Asn Ala  
 115 120 125 130



Asn Met Asn Glu Asp Gly Pro Ser Met Ser Val Asn Phe Thr Ser Pro	135	140	145
Gly Cys Leu Asp His Ile Met Lys Tyr Lys Lys Lys Cys Val Lys Ala	150	155	160
Gly Ser Leu Trp Asp Pro Asn Ile Thr Ala Cys Lys Lys Asn Glu Glu	165	170	175
Thr Val Glu Val Asn Phe Thr Thr Thr Pro Leu Gly Asn Arg Tyr Met	180	185	190
Ala Leu Ile Gln His Ser Thr Ile Ile Gly Phe Ser Gln Val Phe Glu	195	200	205
Pro His Gln Lys Lys Gln Thr Arg Ala Ser Val Val Ile Pro Val Thr	215	220	225
Gly Asp Ser Glu Gly Ala Thr Val Gln Leu Thr Pro Tyr Phe Pro Thr	230	235	240
Cys Gly Ser Asp Cys Ile Arg His Lys Gly Thr Val Val Leu Cys Pro	245	250	255
Gln Thr Gly Val Pro Phe Pro Leu Asp Asn Asn Lys Ser Lys Pro Gly	260	265	270
Gly Trp Leu Pro Leu Leu Leu Leu Ser Leu Leu Val Ala Thr Trp Val	275	280	285
Leu Val Ala Gly Ile Tyr Leu Met Trp Arg His Glu Arg Ile Lys Lys	295	300	305
Thr Ser Phe Ser Thr Thr Thr Leu Leu Pro Pro Ile Lys Val Leu Val	310	315	320
Val Tyr Pro Ser Glu Ile Cys Phe His His Thr Ile Cys Tyr Phe Thr	325	330	335
Glu Phe Leu Gln Asn His Cys Arg Ser Glu Val Ile Leu Glu Lys Trp	340	345	350
Gln Lys Lys Lys Ile Ala Glu Met Gly Pro Val Gln Trp Leu Ala Thr	355	360	365
Gln Lys Lys Ala Ala Asp Lys Val Val Phe Leu Leu Ser Asn Asp Val	375	380	385
Asn Ser Val Cys Asp Gly Thr Cys Gly Lys Ser Glu Gly Ser Pro Ser	390	395	400
Glu Asn Ser Gln Asp Leu Phe Pro Leu Ala Phe Asn Leu Phe Cys Ser	405	410	415
Asp Leu Arg Ser Gln Ile His Leu His Lys Tyr Val Val Val Tyr Phe	420	425	430
Arg Glu Ile Asp Thr Lys Asp Asp Tyr Asn Ala Leu Ser Val Cys Pro	435	440	445
			450

Lys Tyr His Leu Met Lys Asp Ala Thr Ala Phe Cys Ala Glu Leu Leu  
                   455                  460                  465

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 athccnggng ayytnmgnga yytnmgngtn garccngtna cnacnwsngt ngcnacnggn 180  
 gaytaywsna thytnatgaa ygtnwsntgg gtnytnmgng cngaygcnws nathmgnytn 240  
 ytnaargcna cnaarathtg ygtnacnggn aarwsnaayt tycarwsnta ywsntgygtn 300  
 mgntgyaayt ayacngargc nttycaracn caracnmgnc cnwsngggngg naartggacn 360  
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 athccnaayg cnaayatgaa ygargayggn ccnwsnatgw sngtnaaytt yacnwsnccn 480  
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 ggngaywsng arggngcnac ngtnrcarytn acnccntayt tyccnacntg yggnwsngay 780  
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 Gly Gly Ala Asp Leu Lys Gly Asp Tyr Asn Ala Leu Ser Val Cys Pro  
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 Gln Tyr His Leu Met Lys Asp Ala Thr Ala Phe His Thr Glu Leu Leu  
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 Asp Ser Cys Ser Pro Leu  
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 Gln Tyr His Leu Met Lys Asp Ala Thr Ala Phe His Thr Glu Leu Leu  
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atg cct gtg ccc tgg ttc ttg ctg tcc ttg gca ctg ggc cga agc cag 228
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Trp Ile Leu Ser Leu Glu Arg Leu Val Gly Pro Gln Asp Ala Thr His
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tgc tct ccg ggc ctc tcc tgc cgc ctc tgg gac agt gac ata ctc tgc 324
Cys Ser Pro Gly Leu Ser Cys Arg Leu Trp Asp Ser Asp Ile Leu Cys
15 20 25

ctg cct ggg gac atc gtg cct gct ccg ggc ccc gtg ctg gcg cct acg 372
Leu Pro Gly Asp Ile Val Pro Ala Pro Gly Pro Val Leu Ala Pro Thr
30 35 40

cac ctg cag aca gag ctg gtg ctg agg tgc cag aag gag acc gac tgt 420
His Leu Gln Thr Glu Leu Val Leu Arg Cys Gln Lys Glu Thr Asp Cys
45 50 55 60

gac ctc tgt ctg cgt gtg gct gtc cac ttg gcc gtg cat ggg cac tgg 468
Asp Leu Cys Leu Arg Val Ala Val His Leu Ala Val His Gly His Trp
65 70 75

gaa gag cct gaa gat gag gaa aag ttt gga gga gca gct gac tta ggg 516
Glu Glu Pro Glu Asp Glu Glu Lys Phe Gly Gly Ala Ala Asp Leu Gly
80 85 90

gtg gag gag cct agg aat gcc tct ctc cag gcc caa gtc gtg ctc tcc 564
Val Glu Glu Pro Arg Asn Ala Ser Leu Gln Ala Gln Val Val Leu Ser
95 100 105

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Phe Gln Ala Tyr Pro Thr Ala Arg Cys Val Leu Leu Glu Val Gln Val
110 115 120

cct gct gcc ctt gtg cag ttt ggt cag tct gtg ggc tct gtg gta tat 660
Pro Ala Ala Leu Val Gln Phe Gly Gln Ser Val Gly Ser Val Val Tyr
125 130 135 140

gac tgc ttc gag gct gcc cta ggg agt gag gta cga atc tgg tcc tat 708
Asp Cys Phe Glu Ala Ala Leu Gly Ser Glu Val Arg Ile Trp Ser Tyr
145 150 155

act cag ccc agg tac gag aag gaa ctc aac cac aca cag cag ctg cct 756

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Asp	Cys	Arg	Gly	Leu	Glu	Val	Trp	Asn	Ser	Ile	Pro	Ser	Cys	Trp	Ala		
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Pro	Gln	Ile	Ile	Thr	Leu	Asn	His	Thr	Asp	Leu	Val	Pro	Cys	Leu	Cys		
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Pro	Cys	Gln	Pro	Leu	Val	Pro	Pro	Leu	Ser	Trp	Glu	Asn	Val	Thr	Val		
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Asp	Ser	Leu	Gly	Pro	Leu	Lys	Asp	Asp	Val	Leu	Leu	Leu	Glu	Thr	Arg		
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Gly	Pro	Gln	Asp	Asn	Arg	Ser	Leu	Cys	Ala	Leu	Glu	Pro	Ser	Gly	Cys		
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Thr	Ser	Leu	Pro	Ser	Lys	Ala	Ser	Thr	Arg	Ala	Ala	Arg	Leu	Gly	Glu		
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Lys	Arg	Trp	Ala	Leu	Val	Trp	Leu	Ala	Cys	Leu	Leu	Phe	Ala	Ala	Ala		
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gcg	gct	ctg	ctc	ctc	tac	tca	gcc	gat	gac	tcg	ggt	ttc	gag	cgc	ctg	1716	
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Val	Asp	Leu	Trp	Ser	Arg	Arg	Glu	Leu	Ser	Ala	Gln	Gly	Pro	Val	Ala		
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Gln	Asp	Gly	Val	Ser	Gly	Pro	Gly	Ala	His	Gly	Pro	His	Asp	Ala	Phe		
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Pro	Gly	Ser	Tyr	Val	Gly	Ala	Cys	Phe	Asp	Arg	Leu	Leu	His	Pro	Asp		
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gcc	gta	ccc	gcc	ctt	ttc	cgc	acc	gtg	ccc	gtc	ttc	aca	ctg	ccc	ttc	2100	
Ala	Val	Pro	Ala	Leu	Phe	Arg	Thr	Val	Pro	Val	Phe	Thr	Leu	Pro	Ser		
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Gln	Leu	Pro	Asp	Phe	Leu	Gly	Ala	Leu	Gln	Gln	Pro	Arg	Ala	Pro	Arg		
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 cca gcc ctg gat agc tac ttc cat ccc ccg ggg acn tcc gcg ccg gga 2244  
 Pro Ala Leu Asp Ser Tyr Phe His Pro Pro Gly Xaa Ser Ala Pro Gly  
 655 660 665  
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 His Leu Gln Thr Glu Leu Val Leu Arg Cys Gln Lys Glu Thr Asp Cys  
 45 50 55 60  
 Asp Leu Cys Leu Arg Val Ala Val His Leu Ala Val His Gly His Trp  
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 Glu Glu Pro Glu Asp Glu Glu Lys Phe Gly Gly Ala Ala Asp Leu Gly  
 80 85 90  
 Val Glu Glu Pro Arg Asn Ala Ser Leu Gln Ala Gln Val Val Leu Ser  
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 Phe Gln Ala Tyr Pro Thr Ala Arg Cys Val Leu Leu Glu Val Gln Val  
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 Pro Ala Ala Leu Val Gln Phe Gly Gln Ser Val Gly Ser Val Val Tyr  
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 Asp Cys Phe Glu Ala Ala Leu Gly Ser Glu Val Arg Ile Trp Ser Tyr  
 145 150 155  
 Thr Gln Pro Arg Tyr Glu Lys Glu Leu Asn His Thr Gln Gln Leu Pro  
 160 165 170  
 Asp Cys Arg Gly Leu Glu Val Trp Asn Ser Ile Pro Ser Cys Trp Ala  
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Leu Asn Val Ser Glu Glu Gln His Phe Gly Leu Ser Leu Tyr Trp Asn		
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Gln Val Gln Gly Pro Pro Lys Pro Arg Trp His Lys Asn Leu Thr Gly		
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Pro Gln Ile Ile Thr Leu Asn His Thr Asp Leu Val Pro Cys Leu Cys		
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Ile Gln Val Trp Pro Leu Glu Pro Asp Ser Val Arg Thr Asn Ile Cys		
	255	260 265
Pro Phe Arg Glu Asp Pro Arg Ala His Gln Asn Leu Trp Gln Ala Ala		
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Ser Leu Pro Ala Glu Ala Ala Leu Cys Trp Arg Ala Pro Gly Gly Asp		
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Pro Cys Gln Pro Leu Val Pro Pro Leu Ser Trp Glu Asn Val Thr Val		
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Asp Val Asn Ser Ser Glu Lys Leu Gln Leu Gln Glu Cys Leu Trp Ala		
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Asp Ser Leu Gly Pro Leu Lys Asp Asp Val Leu Leu Leu Glu Thr Arg		
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Gly Pro Gln Asp Asn Arg Ser Leu Cys Ala Leu Glu Pro Ser Gly Cys		
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Thr Ser Leu Pro Ser Lys Ala Ser Thr Arg Ala Ala Arg Leu Gly Glu		
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Tyr Leu Leu Gln Asp Leu Gln Ser Gly Gln Cys Leu Gln Leu Trp Asp		
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Asp Asp Leu Gly Ala Leu Trp Ala Cys Pro Met Asp Lys Tyr Ile His		
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Lys Arg Trp Ala Leu Val Trp Leu Ala Cys Leu Leu Phe Ala Ala Ala		
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Arg Leu Leu Lys Gln Asp Val Arg Ser Gly Ala Ala Ala Arg Gly Arg		
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Ala Ala Leu Leu Leu Tyr Ser Ala Asp Asp Ser Gly Phe Glu Arg Leu		
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Val Gly Ala Leu Ala Ser Ala Leu Cys Gln Leu Pro Leu Arg Val Ala		
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Val Asp Leu Trp Ser Arg Arg Glu Leu Ser Ala Gln Gly Pro Val Ala		

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Trp Phe His Ala Gln Arg Arg Gln Thr Leu Gln Glu Gly Gly Val Val		
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Val Leu Leu Phe Ser Pro Gly Ala Val Ala Leu Cys Ser Glu Trp Leu		
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Gln Asp Gly Val Ser Gly Pro Gly Ala His Gly Pro His Asp Ala Phe		
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Arg Ala Ser Leu Ser Cys Val Leu Pro Asp Phe Leu Gln Gly Arg Ala		
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Pro Gly Ser Tyr Val Gly Ala Cys Phe Asp Arg Leu Leu His Pro Asp		
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Ala Val Pro Ala Leu Phe Arg Thr Val Pro Val Phe Thr Leu Pro Ser		
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Gln Leu Pro Asp Phe Leu Gly Ala Leu Gln Gln Pro Arg Ala Pro Arg		
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Ser Gly Arg Leu Gln Glu Arg Ala Glu Gln Val Ser Arg Ala Leu Gln		
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&lt;211&gt; 2109

&lt;212&gt; DNA

&lt;213&gt; reverse translation

&lt;220&gt;

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&lt;222&gt; (1)..(2109)

&lt;223&gt; n may be a, c, g, or t

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 aaywsnathc cnwsntgytg ggcnytnccn tggytnaayg tnwsngenga yggngayaay 660  
 gtncayytng tnytnaaygt nwsngargar carcayttyg gnytnwsnyt ntaytggaay 720  
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<222> (259)..(2292)

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Glu Leu Gln Glu Ser Arg Asn Ala Ser Leu Gln Ala Gln Val Val Leu
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Ser Phe Gln Ala Tyr Pro Ile Ala Arg Cys Ala Leu Leu Glu Val Gln
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Val Pro Ala Asp Leu Val Gln Pro Gly Gln Ser Val Gly Ser Ala Val
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Trp Ala Asp Ser Leu Gly Pro Phe Lys Asp Asp Met Leu Leu Val Glu	
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Ala Ala Ala Leu Phe Phe Phe Leu Leu Leu Lys Lys Asp Arg Arg Lys	
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Ala Ala Arg Gly Ser Arg Thr Ala Leu Leu Leu His Ser Ala Asp Gly	
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Ala Gly Tyr Glu Arg Leu Val Gly Ala Leu Ala Ser Ala Leu Ser Gln	
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Met Pro Leu Arg Val Ala Val Asp Leu Trp Ser Arg Arg Glu Leu Ser	
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Gln Glu Gly Gly Val Val Ile Leu Leu Phe Ser Pro Ala Ala Val Ala	
540 545 550	
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Gln Cys Gln Gln Trp Leu Gln Leu Gln Thr Val Glu Pro Gly Pro His	
555 560 565	
gac gcc ctc gcc gcc tgg ctc agc tgc gtg cta ccc gat ttc ctg caa	2007
Asp Ala Leu Ala Ala Trp Leu Ser Cys Val Leu Pro Asp Phe Leu Gln	
570 575 580	
ggc cgg gcg acc ggc cgc tac gtc ggg gtc tac ttc gac ggg ctg ctg	2055
Gly Arg Ala Thr Gly Arg Tyr Val Gly Val Tyr Phe Asp Gly Leu Leu	
585 590 595	
cac cca gac tct gtg ccc tcc ccg ttc cgc gtc gcc ccg ctc ttc tcc	2103
His Pro Asp Ser Val Pro Ser Pro Phe Arg Val Ala Pro Leu Phe Ser	
600 605 610 615	

ctg ccc tcg cag ctg ccg gct ttc ctg gat gca ctg cag gga ggc tgc 2151  
 Leu Pro Ser Gln Leu Pro Ala Phe Leu Asp Ala Leu Gln Gly Gly Cys  
                     620                    625                    630

tcc act tcc gcg ggg cga ccc gcg gac cgg gtg gaa cga gtg acc cag 2199  
 Ser Thr Ser Ala Gly Arg Pro Ala Asp Arg Val Glu Arg Val Thr Gln  
                     635                    640                    645

gcg ctg cgg tcc gcc ctg gac agc tgt act tct agc tcg gaa gcc cca 2247  
 Ala Leu Arg Ser Ala Leu Asp Ser Cys Thr Ser Ser Ser Glu Ala Pro  
                     650                    655                    660

ggc tgc tgc gag gaa tgg gac ctg gga ccc tgc act aca cta gaa 2292  
 Gly Cys Cys Glu Glu Trp Asp Leu Gly Pro Cys Thr Thr Leu Glu  
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taaaagccga tacagtattc ct 2314

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Val Val Val Ser Leu Glu Arg Leu Met Glu Pro Gln Asp Thr Ala Arg  
                     -1    1                    5                    10

Cys Ser Leu Gly Leu Ser Cys His Leu Trp Asp Gly Asp Val Leu Cys  
                     15                    20                    25

Leu Pro Gly Ser Leu Gln Ser Ala Pro Gly Pro Val Leu Val Pro Thr  
                     30                    35                    40

Arg Leu Gln Thr Glu Leu Val Leu Arg Cys Pro Gln Lys Thr Asp Cys  
                     45                    50                    55                    60

Ala Leu Cys Val Arg Val Val Val His Leu Ala Val His Gly His Trp  
                     65                    70                    75

Ala Glu Pro Glu Glu Ala Gly Lys Ser Asp Ser Glu Leu Gln Glu Ser  
                     80                    85                    90

Arg Asn Ala Ser Leu Gln Ala Gln Val Val Leu Ser Phe Gln Ala Tyr  
                     95                    100                    105

Pro Ile Ala Arg Cys Ala Leu Leu Glu Val Gln Val Pro Ala Asp Leu  
                     110                    115                    120

Val Gln Pro Gly Gln Ser Val Gly Ser Ala Val Phe Asp Cys Phe Glu  
                     125                    130                    135                    140

Ala Ser Leu Gly Ala Glu Val Gln Ile Trp Ser Tyr Thr Lys Pro Arg  
                     145                    150                    155

Tyr Gln Lys Glu Leu Asn Leu Thr Gln Gln Leu Pro Asp Cys Arg Gly

160	165	170
Leu Glu Val Arg Asp Ser Ile Gln Ser Cys Trp Val Leu Pro Trp Leu		
175	180	185
Asn Val Ser Thr Asp Gly Asp Asn Val Leu Leu Thr Leu Asp Val Ser		
190	195	200
Glu Glu Gln Asp Phe Ser Phe Leu Leu Tyr Leu Arg Pro Val Pro Asp		
205	210	215
220		
Ala Leu Lys Ser Leu Trp Tyr Lys Asn Leu Thr Gly Pro Gln Asn Ile		
225	230	235
Thr Leu Asn His Thr Asp Leu Val Pro Cys Leu Cys Ile Gln Val Trp		
240	245	250
Ser Leu Glu Pro Asp Ser Glu Arg Val Glu Phe Cys Pro Phe Arg Glu		
255	260	265
Asp Pro Gly Ala His Arg Asn Leu Trp His Ile Ala Arg Leu Arg Val		
270	275	280
Leu Ser Pro Gly Val Trp Gln Leu Asp Ala Pro Cys Cys Leu Pro Gly		
285	290	295
300		
Lys Val Thr Leu Cys Trp Gln Ala Pro Asp Gln Ser Pro Cys Gln Pro		
305	310	315
Leu Val Pro Pro Val Pro Gln Lys Asn Ala Thr Val Asn Glu Pro Gln		
320	325	330
Asp Phe Gln Leu Val Ala Gly His Pro Asn Leu Cys Val Gln Val Ser		
335	340	345
Thr Trp Glu Lys Val Gln Leu Gln Ala Cys Leu Trp Ala Asp Ser Leu		
350	355	360
Gly Pro Phe Lys Asp Asp Met Leu Leu Val Glu Met Lys Thr Gly Leu		
365	370	375
380		
Asn Asn Thr Ser Val Cys Ala Leu Glu Pro Ser Gly Cys Thr Pro Leu		
385	390	395
Pro Ser Met Ala Ser Thr Arg Ala Ala Arg Leu Gly Glu Glu Leu Leu		
400	405	410
Gln Asp Phe Arg Ser His Gln Cys Met Gln Leu Trp Asn Asp Asp Asn		
415	420	425
Met Gly Ser Leu Trp Ala Cys Pro Met Asp Lys Tyr Ile His Arg Arg		
430	435	440
Trp Val Leu Val Trp Leu Ala Cys Leu Leu Leu Ala Ala Ala Leu Phe		
445	450	455
460		
Phe Phe Leu Leu Leu Lys Lys Asp Arg Arg Lys Ala Ala Arg Gly Ser		
465	470	475
Arg Thr Ala Leu Leu Leu His Ser Ala Asp Gly Ala Gly Tyr Glu Arg		



480	485	490
Leu Val Gly Ala Leu Ala Ser Ala Leu Ser Gln Met Pro Leu Arg Val 495	500	505
Ala Val Asp Leu Trp Ser Arg Arg Glu Leu Ser Ala His Gly Ala Leu 510	515	520
Ala Trp Phe His His Gln Arg Arg Arg Ile Leu Gln Glu Gly Gly Val 525	530	535 540
Val Ile Leu Leu Phe Ser Pro Ala Ala Val Ala Gln Cys Gln Gln Trp 545	550	555
Leu Gln Leu Gln Thr Val Glu Pro Gly Pro His Asp Ala Leu Ala Ala 560	565	570
Trp Leu Ser Cys Val Leu Pro Asp Phe Leu Gln Gly Arg Ala Thr Gly 575	580	585
Arg Tyr Val Gly Val Tyr Phe Asp Gly Leu Leu His Pro Asp Ser Val 590	595	600
Pro Ser Pro Phe Arg Val Ala Pro Leu Phe Ser Leu Pro Ser Gln Leu 605	610	615 620
Pro Ala Phe Leu Asp Ala Leu Gln Gly Gly Cys Ser Thr Ser Ala Gly 625	630	635
Arg Pro Ala Asp Arg Val Glu Arg Val Thr Gln Ala Leu Arg Ser Ala 640	645	650
Leu Asp Ser Cys Thr Ser Ser Ser Glu Ala Pro Gly Cys Cys Glu Glu 655	660	665
Trp Asp Leu Gly Pro Cys Thr Thr Leu Glu 670	675	

&lt;210&gt; 12

&lt;211&gt; 2094

&lt;212&gt; DNA

&lt;213&gt; reverse translation

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)..(2094)

&lt;223&gt; n may be a, c, g, or t

&lt;400&gt; 12

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ytngarmgny tnatggarcc ncargayacn gcnmgntgyw snytnggnyt nwsntgycay 120

ytntgggayg gngaygtnyt ntgyytncn ggnwsnytn arwsngcncc nggncngtn 180

ytngtnccna cnmgnytnca racngarytn gtntnmgnt gyccncaraa racngaytgy 240

gcnytnrgyg tnmngntngt ngtncaaytn gcngtncaayg gncaytgggc ngarccngar 300

gargcnggna arwsngayws ngarytnicar garwsnmgna aygcnwsnyt ncargncar 360  
 gtngtnytnw snttycargc ntayccnath gcnmgntgyg cnytnytnga rgtncargtn 420  
 ccngcngayy tngtncarcc nggncarwsn gtnggnwsng cngtnttyga ytgtytygar 480  
 gcnwsnytnng gngcngargt ncarathtg wstnayacna arccnmngta ycaraargar 540  
 ytnaayytina cncarcaryt nccngaytgy mgnggnytnng argtnmgnga ywsnathcar 600  
 wsntgytggg tnytnccntg gytnaaygt nwsnacngayg gngayaaygt nytnytnacn 660  
 ytngaygt nwsngargar rgaraytywsn tyytntnytn ayytnmgnc ngtnccngay 720  
 gcnytnaarw snytntggt yaaraayytin acnggncnc araayathac nytnaaycay 780  
 acngayytng tncntgyt ntgyathcar gtntggwsny tngarccnga ywsngarmgn 840  
 gtngarttyt gyccnttymg ngargayccn ggngcncaym gnaayytntg gcayathgcn 900  
 mgnytnmgng tnytnwsncc ngngnttg carytngayg cncntgytg yytnccnggn 960  
 aargtnacny tntgytggca rgncncngay carwsnccnt gycarccnyt ngtnccncn 1020  
 gtncncara araaygcnc ngtnaaygar ccncargayt tycarytngt ngcnggncay 1080  
 ccnaayytnt gygtncargt nwsnacntgg garaargtnc arytncargc ntgyytntg 1140  
 gcngaywsny tnggncntt yaargaygay atgytnytng tngaratgaa racnggnytn 1200  
 aayaayacnw sngtntgygc nytngarccn wnggntgya cncnytncc nwsnatggcn 1260  
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 atgcarytnt ggaaygayga yaayatgggn wsnytntgg cntgyccnat ggayaartay 1380  
 athcaymgm gntgggtnyt ngtntggytn gcntgytnt tnytngcngc ngcnytnnt 1440  
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 cayggngcny tngcntggt ycaycaycar mgmngmngna thytncarga rggngngtn 1680  
 gtnathytn tnttywsncc ngcngcngtn gncartgyc arcartggyt ncarytnicar 1740  
 acngtnarc cnggncnc yaaygcnytn gcngcntggy tnwsntgyt nytnccngay 1800  
 tyytncarg gnmngcnc nggngntay gtngngnt aytygaygg nytnytnacay 1860  
 ccngaywsng tncnwsncc nttymgntn gncnytn tywsnytncc nwsncarytn 1920  
 ccngcntty tngaygcnyt ncarggnggn tgywsnacnw sngcngngm nccngcngay 1980  
 mgngtnarm gngtnacna rgcnytnmg wsgcnytn aywsntgyac nwsnwsnwsn 2040  
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<220>  
 <223> Description of Unknown Organism:primate; surmised  
 Homo sapiens

<220>  
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 <222> (70)..(2283)

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<220>  
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 <222> (9)..(134)  
 <223> Xaa translation (9, 18,26, 109,120, 134) depends  
 on genetic code

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 cgacacggcc atg gcc ccg tgg ctg cag ctc tgc tcc gtc ttc ttt acg gtc 111  
 Met Ala Pro Trp Leu Gln Leu Cys Ser Val Phe Phe Thr Val  
 -15 -10 -5  
 aac gcc tgc ctc aac ggc tcg cag ctg gct gtn gcc gct ggc ggg tcc 159  
 Asn Ala Cys Leu Asn Gly Ser Gln Leu Ala Xaa Ala Ala Gly Gly Ser  
 -1 1 5 10  
 ggc cgc gcg cng ggc gcc gac acc tgt agc tgg ang gga gtg ggg cca 207  
 Gly Arg Ala Xaa Gly Ala Asp Thr Cys Ser Trp Xaa Gly Val Gly Pro  
 15 20 25 30  
 gcc agc aga aac agt ggg ctg tac aac atc acc ttc aaa tat gac aat 255  
 Ala Ser Arg Asn Ser Gly Leu Tyr Asn Ile Thr Phe Lys Tyr Asp Asn  
 35 40 45  
 tgt acc acc tac ttg aat cca gtg ggg aag cat gtg att gct gac gcc 303  
 Cys Thr Thr Tyr Leu Asn Pro Val Gly Lys His Val Ile Ala Asp Ala  
 50 55 60  
 cag aat atc acc atc agc cag tat gct tgc cat gac caa gtg gca gtc 351  
 Gln Asn Ile Thr Ile Ser Gln Tyr Ala Cys His Asp Gln Val Ala Val  
 65 70 75  
 acc att ctt tgg tcc cca ggg gcc ctc ggc atc gaa ttc ctg aaa gga 399  
 Thr Ile Leu Trp Ser Pro Gly Ala Leu Gly Ile Glu Phe Leu Lys Gly  
 80 85 90  
 ttt cgg gta ata ctg gag gag ctg aag tcg gag gga aga cag ngc caa 447  
 Phe Arg Val Ile Leu Glu Glu Leu Lys Ser Glu Gly Arg Gln Xaa Gln  
 95 100 105 110  
 caa ctg att cta aag gat ccg aag cag ntc aac agt agc ttc aaa aga 495

Gln	Leu	Ile	Leu	Lys	Asp	Pro	Lys	Gln	Xaa	Asn	Ser	Ser	Phe	Lys	Arg	
				115					120					125		
act	gga	atg	gaa	tct	caa	cct	ttn	ctg	aat	atg	aaa	ttt	gaa	acg	gat	543
Thr	Gly	Met	Glu	Ser	Gln	Pro	Xaa	Leu	Asn	Met	Lys	Phe	Glu	Thr	Asp	
			130					135					140			
tat	ttc	gta	agg	ttg	tcc	ttt	tcc	ttc	att	aaa	aac	gaa	agc	aat	tac	591
Tyr	Phe	Val	Arg	Leu	Ser	Phe	Ser	Phe	Ile	Lys	Asn	Glu	Ser	Asn	Tyr	
		145					150					155				
cac	cct	ttc	ttc	ttt	aga	acc	cga	gcc	tgt	gac	ctg	ttg	tta	cag	ccg	639
His	Pro	Phe	Phe	Phe	Arg	Thr	Arg	Ala	Cys	Asp	Leu	Leu	Leu	Gln	Pro	
	160					165					170					
gac	aat	cta	gct	tgt	aaa	ccc	ttc	tgg	aag	cct	cgg	aac	ctg	aac	atc	687
Asp	Asn	Leu	Ala	Cys	Lys	Pro	Phe	Trp	Lys	Pro	Arg	Asn	Leu	Asn	Ile	
175					180					185					190	
agc	cag	cat	ggc	tcg	gac	atg	cag	gtg	tcc	ttc	gac	cac	gca	ccg	cac	735
Ser	Gln	His	Gly	Ser	Asp	Met	Gln	Val	Ser	Phe	Asp	His	Ala	Pro	His	
				195				200					205			
aac	ttc	ggc	ttc	cgt	ttc	ttc	tat	ctt	cac	tac	aag	ctc	aag	cac	gaa	783
Asn	Phe	Gly	Phe	Arg	Phe	Phe	Tyr	Leu	His	Tyr	Lys	Leu	Lys	His	Glu	
		210					215					220				
gga	cct	ttc	aag	cga	aag	acc	tgt	aag	cag	gag	caa	act	aca	gag	atg	831
Gly	Pro	Phe	Lys	Arg	Lys	Thr	Cys	Lys	Gln	Glu	Gln	Thr	Thr	Glu	Met	
	225					230						235				
acc	agc	tgc	ctc	ctt	caa	aat	gtt	tct	cca	ggg	gat	tat	ata	att	gag	879
Thr	Ser	Cys	Leu	Leu	Gln	Asn	Val	Ser	Pro	Gly	Asp	Tyr	Ile	Ile	Glu	
	240				245						250					
ctg	gtg	gat	gac	act	aac	aca	aca	aga	aaa	gtg	atg	cat	tat	gcc	tta	927
Leu	Val	Asp	Asp	Thr	Asn	Thr	Thr	Arg	Lys	Val	Met	His	Tyr	Ala	Leu	
255					260					265					270	
aag	cca	gtg	cac	tcc	ccg	tgg	gcc	ggg	ccc	atc	aga	gcc	gtg	gcc	atc	975
Lys	Pro	Val	His	Ser	Pro	Trp	Ala	Gly	Pro	Ile	Arg	Ala	Val	Ala	Ile	
				275				280					285			
aca	gtg	cca	ctg	gta	gtc	ata	tcg	gca	ttc	gcg	acg	ctc	ttc	act	gtg	1023
Thr	Val	Pro	Leu	Val	Val	Ile	Ser	Ala	Phe	Ala	Thr	Leu	Phe	Thr	Val	
			290					295					300			
atg	tgc	cgc	aag	aag	caa	caa	gaa	aat	ata	tat	tca	cat	tta	gat	gaa	1071
Met	Cys	Arg	Lys	Lys	Gln	Gln	Glu	Asn	Ile	Tyr	Ser	His	Leu	Asp	Glu	
	305						310					315				
gag	agc	tct	gag	tct	tcc	aca	tac	act	gca	gca	ctc	cca	aga	gag	agg	1119
Glu	Ser	Ser	Glu	Ser	Ser	Thr	Tyr	Thr	Ala	Ala	Leu	Pro	Arg	Glu	Arg	
	320					325					330					
ctc	cgg	ccg	cgg	ccg	aag	gtc	ttt	ctc	tgc	tat	tcc	agt	aaa	gat	ggc	1167
Leu	Arg	Pro	Arg	Pro	Lys	Val	Phe	Leu	Cys	Tyr	Ser	Ser	Lys	Asp	Gly	
335					340				345					350		
cag	aat	cac	atg	aat	gtc	gtc	cag	tgt	ttc	gcc	tac	ttc	ctc	cag	gac	1215

Gln	Asn	His	Met	Asn	Val	Val	Gln	Cys	Phe	Ala	Tyr	Phe	Leu	Gln	Asp		
			355						360					365			
ttc	tgt	ggc	tgt	gag	gtg	gct	ctg	gac	ctg	tgg	gaa	gac	ttc	agc	ctc	1263	
Phe	Cys	Gly	Cys	Glu	Val	Ala	Leu	Asp	Leu	Trp	Glu	Asp	Phe	Ser	Leu		
			370					375					380				
tgt	aga	gaa	ggg	cag	aga	gaa	tgg	gtc	atc	cag	aag	atc	cac	gag	tcc	1311	
Cys	Arg	Glu	Gly	Gln	Arg	Glu	Trp	Val	Ile	Gln	Lys	Ile	His	Glu	Ser		
		385					390					395					
cag	ttc	atc	att	gtg	gtt	tgt	tcc	aaa	ggt	atg	aag	tac	ttt	gtg	gac	1359	
Gln	Phe	Ile	Ile	Val	Val	Cys	Ser	Lys	Gly	Met	Lys	Tyr	Phe	Val	Asp		
	400					405					410						
aag	aag	aac	tac	aaa	cac	aaa	gga	ggt	ggc	cga	ggc	tcg	ggg	aaa	gga	1407	
Lys	Lys	Asn	Tyr	Lys	His	Lys	Gly	Gly	Gly	Arg	Gly	Ser	Gly	Lys	Gly		
415				420						425				430			
gag	ctc	ttc	ctg	gtg	gcg	gtg	tca	gcc	att	gcc	gaa	aag	ctc	cgc	cag	1455	
Glu	Leu	Phe	Leu	Val	Ala	Val	Ser	Ala	Ile	Ala	Glu	Lys	Leu	Arg	Gln		
			435					440						445			
gcc	aag	cag	agt	tcg	tcc	gcg	gcg	ctc	agc	aag	ttt	atc	gcc	gtc	tac	1503	
Ala	Lys	Gln	Ser	Ser	Ser	Ala	Ala	Leu	Ser	Lys	Phe	Ile	Ala	Val	Tyr		
		450						455					460				
ttt	gat	tat	tcc	tgc	gag	gga	gac	gtc	ccc	ggt	atc	cta	gac	ctg	agt	1551	
Phe	Asp	Tyr	Ser	Cys	Glu	Gly	Asp	Val	Pro	Gly	Ile	Leu	Asp	Leu	Ser		
	465					470					475						
acc	aag	tac	aga	ctc	atg	gac	aat	ctt	cct	cag	ctc	tgt	tcc	cac	ctg	1599	
Thr	Lys	Tyr	Arg	Leu	Met	Asp	Asn	Leu	Pro	Gln	Leu	Cys	Ser	His	Leu		
	480					485					490						
cac	tcc	cga	gac	cac	ggc	ctc	cag	gag	ccg	ggg	cag	cac	acg	cga	cag	1647	
His	Ser	Arg	Asp	His	Gly	Leu	Gln	Glu	Pro	Gly	Gln	His	Thr	Arg	Gln		
495					500					505				510			
ggc	agc	aga	agg	aac	tac	ttc	cgg	agc	aag	tca	ggc	cgg	tcc	cta	tac	1695	
Gly	Ser	Arg	Arg	Asn	Tyr	Phe	Arg	Ser	Lys	Ser	Gly	Arg	Ser	Leu	Tyr		
			515						520					525			
gtc	gcc	att	tgc	aac	atg	cac	cag	ttt	att	gac	gag	gag	ccc	gac	tgg	1743	
Val	Ala	Ile	Cys	Asn	Met	His	Gln	Phe	Ile	Asp	Glu	Glu	Pro	Asp	Trp		
		530						535					540				
ttc	gaa	aag	cag	ttc	gtt	ccc	ttc	cat	cct	cct	cca	ctg	cgc	tac	cgg	1791	
Phe	Glu	Lys	Gln	Phe	Val	Pro	Phe	His	Pro	Pro	Pro	Leu	Arg	Tyr	Arg		
		545					550					555					
gag	cca	gtc	ttg	gag	aaa	ttt	gat	tcg	ggc	ttg	gtt	tta	aat	gat	gtc	1839	
Glu	Pro	Val	Leu	Glu	Lys	Phe	Asp	Ser	Gly	Leu	Val	Leu	Asn	Asp	Val		
	560					565					570						
atg	tgc	aaa	cca	ggg	cct	gag	agt	gac	ttc	tgc	cta	aag	gta	gag	gcg	1887	
Met	Cys	Lys	Pro	Gly	Pro	Glu	Ser	Asp	Phe	Cys	Leu	Lys	Val	Glu	Ala		
575					580					585				590			
gct	gtt	ctt	ggg	gca	acc	gga	cca	gcc	gac	tcc	cag	cac	gag	agt	cag	1935	

Ala Val Leu Gly	Ala Thr Gly Pro Ala Asp Ser Gln His Glu Ser Gln	
	595 600 605	
cat ggg ggc ctg gac caa gac ggg gag gcc cgg cct gcc ctt gac ggt	1983	
His Gly Gly Leu Asp Gln Asp Gly Glu Ala Arg Pro Ala Leu Asp Gly		
	610 615 620	
agc gcc gcc ctg caa ccc ctg ctg cac acg gtg aaa gcc ggc agc ccc	2031	
Ser Ala Ala Leu Gln Pro Leu Leu His Thr Val Lys Ala Gly Ser Pro		
	625 630 635	
tcg gac atg ccg cgg gac tca ggc atc tat gac tcg tct gtg ccc tca	2079	
Ser Asp Met Pro Arg Asp Ser Gly Ile Tyr Asp Ser Ser Val Pro Ser		
	640 645 650	
tcc gag ctg tct ctg cca ctg atg gaa gga ctc tcg acg gac cag aca	2127	
Ser Glu Leu Ser Leu Pro Leu Met Glu Gly Leu Ser Thr Asp Gln Thr		
	655 660 665 670	
gaa acg tct tcc ctg acg gag agc gtg tcc tcc tct tca ggc ctg ggt	2175	
Glu Thr Ser Ser Leu Thr Glu Ser Val Ser Ser Ser Ser Gly Leu Gly		
	675 680 685	
gag gag gaa cct cct gcc ctt cct tcc aag ctc ctc tct tct ggg tca	2223	
Glu Glu Glu Pro Pro Ala Leu Pro Ser Lys Leu Leu Ser Ser Gly Ser		
	690 695 700	
tgc aaa gca gat ctt ggt tgc cgc agc tac act gat gaa ctc cac gcg	2271	
Cys Lys Ala Asp Leu Gly Cys Arg Ser Tyr Thr Asp Glu Leu His Ala		
	705 710 715	
gtc gcc cct ttg taacaaaacg aaagagtcta agcattgcc a ttttagctgc	2323	
Val Ala Pro Leu		
	720	
tgccctccctc tgattcccca gctcatctcc ctgggttgc at ggcccacttg gagctgaggt	2383	
ctcatacaag gatatttgga gtgaaatgct ggccagtact tgtttctccct tgccccaacc	2443	
ctttaccgga tatcttgaca aactctccaa ttttctaaaa tgatatggag ctctgaaagg	2503	
catgtccata aggtctgaca acagcttgcc aaatttggtt agtccttgga tcagagcctg	2563	
ttgtgggagg tagggaggaa atatgtaaag aaaaacagga agatacctgc actaatcatt	2623	
cagacttcat tgagctctgc aaactttgcc tgtttgctat tggctacctt gatttgaaat	2683	
gctttgtgaa aaaaggcact ttttaacatca tagccacaga aatcaagtgc cagtctatct	2743	
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 Ala Xaa Gly Ala Asp Thr Cys Ser Trp Xaa Gly Val Gly Pro Ala Ser  
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 Arg Asn Ser Gly Leu Tyr Asn Ile Thr Phe Lys Tyr Asp Asn Cys Thr  
 35 40 45  
 Thr Tyr Leu Asn Pro Val Gly Lys His Val Ile Ala Asp Ala Gln Asn  
 50 55 60  
 Ile Thr Ile Ser Gln Tyr Ala Cys His Asp Gln Val Ala Val Thr Ile  
 65 70 75 80  
 Leu Trp Ser Pro Gly Ala Leu Gly Ile Glu Phe Leu Lys Gly Phe Arg  
 85 90 95  
 Val Ile Leu Glu Glu Leu Lys Ser Glu Gly Arg Gln Xaa Gln Gln Leu  
 100 105 110  
 Ile Leu Lys Asp Pro Lys Gln Xaa Asn Ser Ser Phe Lys Arg Thr Gly  
 115 120 125  
 Met Glu Ser Gln Pro Xaa Leu Asn Met Lys Phe Glu Thr Asp Tyr Phe  
 130 135 140  
 Val Arg Leu Ser Phe Ser Phe Ile Lys Asn Glu Ser Asn Tyr His Pro  
 145 150 155 160  
 Phe Phe Phe Arg Thr Arg Ala Cys Asp Leu Leu Leu Gln Pro Asp Asn  
 165 170 175  
 Leu Ala Cys Lys Pro Phe Trp Lys Pro Arg Asn Leu Asn Ile Ser Gln  
 180 185 190  
 His Gly Ser Asp Met Gln Val Ser Phe Asp His Ala Pro His Asn Phe  
 195 200 205  
 Gly Phe Arg Phe Phe Tyr Leu His Tyr Lys Leu Lys His Glu Gly Pro  
 210 215 220  
 Phe Lys Arg Lys Thr Cys Lys Gln Glu Gln Thr Thr Glu Met Thr Ser  
 225 230 235 240  
 Cys Leu Leu Gln Asn Val Ser Pro Gly Asp Tyr Ile Ile Glu Leu Val  
 245 250 255  
 Asp Asp Thr Asn Thr Thr Arg Lys Val Met His Tyr Ala Leu Lys Pro  
 260 265 270  
 Val His Ser Pro Trp Ala Gly Pro Ile Arg Ala Val Ala Ile Thr Val  
 275 280 285  
 Pro Leu Val Val Ile Ser Ala Phe Ala Thr Leu Phe Thr Val Met Cys  
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 Arg Lys Lys Gln Gln Glu Asn Ile Tyr Ser His Leu Asp Glu Glu Ser  
 305 310 315 320

Ser Glu Ser Ser Thr Tyr Thr Ala Ala Leu Pro Arg Glu Arg Leu Arg  
 325 330 335  
 Pro Arg Pro Lys Val Phe Leu Cys Tyr Ser Ser Lys Asp Gly Gln Asn  
 340 345 350  
 His Met Asn Val Val Gln Cys Phe Ala Tyr Phe Leu Gln Asp Phe Cys  
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 Gly Cys Glu Val Ala Leu Asp Leu Trp Glu Asp Phe Ser Leu Cys Arg  
 370 375 380  
 Glu Gly Gln Arg Glu Trp Val Ile Gln Lys Ile His Glu Ser Gln Phe  
 385 390 395 400  
 Ile Ile Val Val Cys Ser Lys Gly Met Lys Tyr Phe Val Asp Lys Lys  
 405 410 415  
 Asn Tyr Lys His Lys Gly Gly Gly Arg Gly Ser Gly Lys Gly Glu Leu  
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 Gln Ser Ser Ser Ala Ala Leu Ser Lys Phe Ile Ala Val Tyr Phe Asp  
 450 455 460  
 Tyr Ser Cys Glu Gly Asp Val Pro Gly Ile Leu Asp Leu Ser Thr Lys  
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 Tyr Arg Leu Met Asp Asn Leu Pro Gln Leu Cys Ser His Leu His Ser  
 485 490 495  
 Arg Asp His Gly Leu Gln Glu Pro Gly Gln His Thr Arg Gln Gly Ser  
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 Arg Arg Asn Tyr Phe Arg Ser Lys Ser Gly Arg Ser Leu Tyr Val Ala  
 515 520 525  
 Ile Cys Asn Met His Gln Phe Ile Asp Glu Glu Pro Asp Trp Phe Glu  
 530 535 540  
 Lys Gln Phe Val Pro Phe His Pro Pro Pro Leu Arg Tyr Arg Glu Pro  
 545 550 555 560  
 Val Leu Glu Lys Phe Asp Ser Gly Leu Val Leu Asn Asp Val Met Cys  
 565 570 575  
 Lys Pro Gly Pro Glu Ser Asp Phe Cys Leu Lys Val Glu Ala Ala Val  
 580 585 590  
 Leu Gly Ala Thr Gly Pro Ala Asp Ser Gln His Glu Ser Gln His Gly  
 595 600 605  
 Gly Leu Asp Gln Asp Gly Glu Ala Arg Pro Ala Leu Asp Gly Ser Ala  
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 Ala Leu Gln Pro Leu Leu His Thr Val Lys Ala Gly Ser Pro Ser Asp  
 625 630 635 640



Met Pro Arg Asp Ser Gly Ile Tyr Asp Ser Ser Val Pro Ser Ser Glu  
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Leu Ser Leu Pro Leu Met Glu Gly Leu Ser Thr Asp Gln Thr Glu Thr  
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Ser Ser Leu Thr Glu Ser Val Ser Ser Ser Ser Gly Leu Gly Glu Glu  
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Glu Pro Pro Ala Leu Pro Ser Lys Leu Leu Ser Ser Gly Ser Cys Lys  
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Pro Leu

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 tggnnnggng tnggncngc nwsnmgnaay wsnggnytn tayaayathac nttyaartay 180  
 gayaaytgya cnacntayyt naayccngtn ggnaarcayg tnathgcnga ygcncaraay 240  
 athacnathw sncartaygc ntgycaygay cargtngcng tnacnathyt ntggwsnccn 300  
 ggngcnytn gnatggarws ncarccnnnn ytnaayatga arttygarac ngaytaytty 480  
 gtnmgnytnw snttywsntt yathaaraay garwsnaayt aycayccntt yttyttymgn 540  
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 ccnmgnaayy tnaayathws ncarcayggn wsngayatgc argtnwsntt ygaycaygcn 660  
 ccncayaayt tyggnttymg nttyttytay ytncaytaya arytnaarca ygargngcncn 720  
 ttyaarmgna aracntgyaa rcargarcar acnacngara tgacnwsntg yytnytnccar 780  
 aaygtnwsnc cnggngayta yathathgar ytngtngayg ayacnaayac nacnmgnaar 840  
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 taywsnwsna argayggna raaycayatg aaygtngtnc artgyttygc ntayttyytn 1140  
 cargayttyt gyggntgyga rgtngcnytn gayytnnggg argayttyws nytnngymgn 1200  
 garggncarm gngartgggt nathcaraar athcaygarw sncarttyat hathgtngtn 1260  
 tgywsnaarg gnatgaarta yttygtngay aaraaraayt ayaarcayaa rggngngngn 1320  
 mgnggnwsng gnaarggnga rytnttyytn gtngcngtnw sngcnathgc ngaraarytn 1380  
 mgncargcna arcarwsnws nwsngcngcn ytnwsnaart tyathgngt ntayttygay 1440  
 taywsntgyg arggngaygt nccnggnath ytngayytnw snacnaarta ymgnytnatg 1500  
 gayaayytn cncarytnng ywsncayytn caywsnmngn aycayggnyt ncargarcn 1560  
 ggncarcaya cnmgncargg nwsnmngmgn aaytayttym gnwsnaarws nggnmgngn 1620  
 ytnnaygtng cnathtgyaa yatgcaycar ttyathgayg argarcnga ytggttygar 1680  
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 gcnynarc cnytnytnca yacngtnaar gcnggnwsnc cnwsngayat gccnmngay 1980  
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 ytnwsnacng aycaracnga racnwsnwsn ytnacngarw sngtnwsnws nwsnwsngn 2100  
 ytnngngarg argarcncnc ngcnytnccn wsnaarytny tnwsnwsng nwsntgyaar 2160  
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 Homo sapiens

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&lt;222&gt; (70)..(1971)

&lt;400&gt; 16

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Val Ile Asp Leu Ser Asp Ser Ala Gly Ile Gly Phe Arg His Leu Pro	
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cac tgg aac acc cgc tgt cct ctg gcc tcc cac acg gaa gtt ctg cct	144
His Trp Asn Thr Arg Cys Pro Leu Ala Ser His Thr Glu Val Leu Pro	
10 15 20 25	
ata tcc ctt gcc gca cct ggt ggg ccc tct tct cca caa agc ctt ggt	192
Ile Ser Leu Ala Ala Pro Gly Gly Pro Ser Ser Pro Gln Ser Leu Gly	
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Val Cys Glu Ser Gly Thr Val Pro Ala Val Cys Ala Ser Ile Cys Cys	
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cag gtg gct cag gtc ttc aac ggg gcc tct tcc acc tcc tgg tgc aga	288
Gln Val Ala Gln Val Phe Asn Gly Ala Ser Ser Thr Ser Trp Cys Arg	
60 65 70	
aat cca aaa agt ctt cca cat tca agt tct ata gga gac aca aga tgc	336
Asn Pro Lys Ser Leu Pro His Ser Ser Ser Ile Gly Asp Thr Arg Cys	
75 80 85	
cag cac ctg ctc aga gga agc tgc tgc ctc gtc gtc acc tgt ctg aga	384
Gln His Leu Leu Arg Gly Ser Cys Cys Leu Val Val Thr Cys Leu Arg	
90 95 100 105	
aga gcc atc aca ttt cca tcc cct ccc cag aca tct ccc aca agg gac	432
Arg Ala Ile Thr Phe Pro Ser Pro Pro Gln Thr Ser Pro Thr Arg Asp	
110 115 120	
ttc gct cta aaa gga ccc aac ctt cgg atc cag aga cat ggg aaa gtc	480
Phe Ala Leu Lys Gly Pro Asn Leu Arg Ile Gln Arg His Gly Lys Val	
125 130 135	
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Phe Pro Asp Trp Thr His Lys Gly Met Glu Val Gly Thr Gly Tyr Asn	
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agg aga tgg gtt cag ctg agt ggt gga ccc gag ttc tcc ttt gat ttg	576
Arg Arg Trp Val Gln Leu Ser Gly Gly Pro Glu Phe Ser Phe Asp Leu	
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Leu Pro Glu Ala Arg Ala Ile Arg Val Thr Ile Ser Ser Gly Pro Glu	
170 175 180 185	
gtc agc gtg cgt ctt tgt cac cag tgg gca ctg gag tgt gaa gag ctg	672
Val Ser Val Arg Leu Cys His Gln Trp Ala Leu Glu Cys Glu Glu Leu	
190 195 200	

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Ser Ser Pro Tyr Asp Val Gln Lys Ile Val Ser Gly Gly His Thr Val	
205 210 215	
gag ctg cct tat gaa ttc ctt ctg ccc tgt ctg tgc ata gag gca tcc	768
Glu Leu Pro Tyr Glu Phe Leu Leu Pro Cys Leu Cys Ile Glu Ala Ser	
220 225 230	
tac ctg caa gag gac act gtg agg cgc aaa aaa tgt ccc ttc cag agc	816
Tyr Leu Gln Glu Asp Thr Val Arg Arg Lys Lys Cys Pro Phe Gln Ser	
235 240 245	
tgg cca gaa gcc tat ggc tcg gac ttc tgg aag tca gtg cac ttc act	864
Trp Pro Glu Ala Tyr Gly Ser Asp Phe Trp Lys Ser Val His Phe Thr	
250 255 260 265	
gac tac agc cag cac act cag atg gtc atg gcc ctg aca ctc cgc tgc	912
Asp Tyr Ser Gln His Thr Gln Met Val Met Ala Leu Thr Leu Arg Cys	
270 275 280	
cca ctg aag ctg gaa gct gcc ctc tgc cag agg cac gac tgg cat acc	960
Pro Leu Lys Leu Glu Ala Ala Leu Cys Gln Arg His Asp Trp His Thr	
285 290 295	
ctt tgc aaa gac ctc ccg aat gcc acg gct cga gag tca gat ggg tgg	1008
Leu Cys Lys Asp Leu Pro Asn Ala Thr Ala Arg Glu Ser Asp Gly Trp	
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tat gtt ttg gag aag gtg gac ctg cac ccc cag ctc tgc ttc aag gta	1056
Tyr Val Leu Glu Lys Val Asp Leu His Pro Gln Leu Cys Phe Lys Val	
315 320 325	
caa cca tgg ttc tct ttt gga aac agc agc cat gtt gaa tgc ccc cac	1104
Gln Pro Trp Phe Ser Phe Gly Asn Ser Ser His Val Glu Cys Pro His	
330 335 340 345	
cag act ggg tct ctc aca tcc tgg aat gta agc atg gat acc caa gcc	1152
Gln Thr Gly Ser Leu Thr Ser Trp Asn Val Ser Met Asp Thr Gln Ala	
350 355 360	
cag cag ctg att ctt cac ttc tcc tca aga atg cat gcc acc ttc agt	1200
Gln Gln Leu Ile Leu His Phe Ser Ser Arg Met His Ala Thr Phe Ser	
365 370 375	
gct gcc tgg agc ctc cca ggc ttg ggg cag gac act ttg gtg ccc ccc	1248
Ala Ala Trp Ser Leu Pro Gly Leu Gly Gln Asp Thr Leu Val Pro Pro	
380 385 390	
gtg tac act gtc agc cag gtg tgg cgg tca gat gtc cag ttt gcc tgg	1296
Val Tyr Thr Val Ser Gln Val Trp Arg Ser Asp Val Gln Phe Ala Trp	
395 400 405	
aag cac ctc ttg tgt cca gat gtc tct tac aga cac ctg ggg ctc ttg	1344
Lys His Leu Leu Cys Pro Asp Val Ser Tyr Arg His Leu Gly Leu Leu	
410 415 420 425	
atc ctg gca ctg ctg gcc ctc ctc acc cta ctg ggt gtt gtt ctg gcc	1392
Ile Leu Ala Leu Leu Ala Leu Leu Thr Leu Leu Gly Val Val Leu Ala	
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 Leu Thr Cys Arg Arg Pro Gln Ser Gly Pro Gly Pro Ala Arg Pro Val  
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 460 465 470

gcg ctg gct gaa ctg cta cgg gca gcg ctg ggc ggc ggg cgc gac gtg 1536  
 Ala Leu Ala Glu Leu Leu Arg Ala Ala Leu Gly Gly Gly Arg Asp Val  
 475 480 485

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 Ile Val Asp Leu Trp Glu Gly Arg His Val Ala Arg Val Gly Pro Leu  
 490 495 500 505

ccg tgg ctc tgg gcg gcg cgg acg cgc gta gcg cgg gag cag ggc act 1632  
 Pro Trp Leu Trp Ala Ala Arg Thr Arg Val Ala Arg Glu Gln Gly Thr  
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gtg ctg ctg ctg tgg agc ggc gcc gac ctt cgc ccg gtc agc ggc ccc 1680  
 Val Leu Leu Leu Trp Ser Gly Ala Asp Leu Arg Pro Val Ser Gly Pro  
 525 530 535

gac ccc cgc gcc gcg ccc ctg ctc gcc ctg ctc cac gct gcc ccg cgc 1728  
 Asp Pro Arg Ala Ala Pro Leu Leu Ala Leu Leu His Ala Ala Pro Arg  
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ccg ctg ctg ctg ctc gct tac ttc agt cgc ctc tgc gcc aag ggc gac 1776  
 Pro Leu Leu Leu Leu Ala Tyr Phe Ser Arg Leu Cys Ala Lys Gly Asp  
 555 560 565

atc ccc ccg ccg ctg cgc gcc ctg ccg cgc tac cgc ctg ctg cgc gac 1824  
 Ile Pro Pro Pro Leu Arg Ala Leu Pro Arg Tyr Arg Leu Leu Arg Asp  
 570 575 580 585

ctg ccg cgt ctg ctg cgg gcg ctg gac gcg cgg cct ttc gca gag gcc 1872  
 Leu Pro Arg Leu Leu Arg Ala Leu Asp Ala Arg Pro Phe Ala Glu Ala  
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acc agc tgg ggc cgc ctt ggg gcg cgg cag cgc agg cag agc cgc cta 1920  
 Thr Ser Trp Gly Arg Leu Gly Ala Arg Gln Arg Arg Gln Ser Arg Leu  
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gag ctg tgc agc cgg ctc gaa cga gag gcc gcc cga ctt gca gac cta 1968  
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 Ile Ser Leu Ala Ala Pro Gly Gly Pro Ser Ser Pro Gln Ser Leu Gly  
                   30                  35                  40  
 Val Cys Glu Ser Gly Thr Val Pro Ala Val Cys Ala Ser Ile Cys Cys  
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 Gln Val Ala Gln Val Phe Asn Gly Ala Ser Ser Thr Ser Trp Cys Arg  
           60                  65                  70  
 Asn Pro Lys Ser Leu Pro His Ser Ser Ser Ile Gly Asp Thr Arg Cys  
       75                  80                  85  
 Gln His Leu Leu Arg Gly Ser Cys Cys Leu Val Val Thr Cys Leu Arg  
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 Arg Ala Ile Thr Phe Pro Ser Pro Pro Gln Thr Ser Pro Thr Arg Asp  
                   110                  115                  120  
 Phe Ala Leu Lys Gly Pro Asn Leu Arg Ile Gln Arg His Gly Lys Val  
                   125                  130                  135  
 Phe Pro Asp Trp Thr His Lys Gly Met Glu Val Gly Thr Gly Tyr Asn  
       140                  145                  150  
 Arg Arg Trp Val Gln Leu Ser Gly Gly Pro Glu Phe Ser Phe Asp Leu  
       155                  160                  165  
 Leu Pro Glu Ala Arg Ala Ile Arg Val Thr Ile Ser Ser Gly Pro Glu  
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 Val Ser Val Arg Leu Cys His Gln Trp Ala Leu Glu Cys Glu Glu Leu  
                   190                  195                  200  
 Ser Ser Pro Tyr Asp Val Gln Lys Ile Val Ser Gly Gly His Thr Val  
       205                  210                  215  
 Glu Leu Pro Tyr Glu Phe Leu Leu Pro Cys Leu Cys Ile Glu Ala Ser  
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 Tyr Leu Gln Glu Asp Thr Val Arg Arg Lys Lys Cys Pro Phe Gln Ser  
       235                  240                  245  
 Trp Pro Glu Ala Tyr Gly Ser Asp Phe Trp Lys Ser Val His Phe Thr  
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 Asp Tyr Ser Gln His Thr Gln Met Val Met Ala Leu Thr Leu Arg Cys  
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 Pro Leu Lys Leu Glu Ala Ala Leu Cys Gln Arg His Asp Trp His Thr  
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 Leu Cys Lys Asp Leu Pro Asn Ala Thr Ala Arg Glu Ser Asp Gly Trp  
       300                  305                  310

Tyr Val Leu Glu Lys Val Asp Leu His Pro Gln Leu Cys Phe Lys Val  
 315 320 325  
 Gln Pro Trp Phe Ser Phe Gly Asn Ser Ser His Val Glu Cys Pro His  
 330 335 340 345  
 Gln Thr Gly Ser Leu Thr Ser Trp Asn Val Ser Met Asp Thr Gln Ala  
 350 355 360  
 Gln Gln Leu Ile Leu His Phe Ser Ser Arg Met His Ala Thr Phe Ser  
 365 370 375  
 Ala Ala Trp Ser Leu Pro Gly Leu Gly Gln Asp Thr Leu Val Pro Pro  
 380 385 390  
 Val Tyr Thr Val Ser Gln Val Trp Arg Ser Asp Val Gln Phe Ala Trp  
 395 400 405  
 Lys His Leu Leu Cys Pro Asp Val Ser Tyr Arg His Leu Gly Leu Leu  
 410 415 420 425  
 Ile Leu Ala Leu Leu Ala Leu Leu Thr Leu Leu Gly Val Val Leu Ala  
 430 435 440  
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 445 450 455  
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 460 465 470  
 Ala Leu Ala Glu Leu Leu Arg Ala Ala Leu Gly Gly Gly Arg Asp Val  
 475 480 485  
 Ile Val Asp Leu Trp Glu Gly Arg His Val Ala Arg Val Gly Pro Leu  
 490 495 500 505  
 Pro Trp Leu Trp Ala Ala Arg Thr Arg Val Ala Arg Glu Gln Gly Thr  
 510 515 520  
 Val Leu Leu Leu Trp Ser Gly Ala Asp Leu Arg Pro Val Ser Gly Pro  
 525 530 535  
 Asp Pro Arg Ala Ala Pro Leu Leu Ala Leu Leu His Ala Ala Pro Arg  
 540 545 550  
 Pro Leu Leu Leu Leu Ala Tyr Phe Ser Arg Leu Cys Ala Lys Gly Asp  
 555 560 565  
 Ile Pro Pro Pro Leu Arg Ala Leu Pro Arg Tyr Arg Leu Leu Arg Asp  
 570 575 580 585  
 Leu Pro Arg Leu Leu Arg Ala Leu Asp Ala Arg Pro Phe Ala Glu Ala  
 590 595 600  
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Gly

<210> 18  
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gcwnsncaaya cngargtnyt nccnathwsn ytngcngcnc cnggnggncc nwsnwsnccn 180  
carwsnytnng gngtntgyga rwsnggnacn gtnccngcng tntgygcnws nathtgytgy 240  
cargtngcnc argtnttyaa yggngcnwsn wsnacnwsnt ggtgymgnaa yccnaarwsn 300  
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carytnwsng gnggnccnga rtywsntty gayytnytn cngargcnmg ngcnathmgn 600  
gtnacnathw snwsnggncc ngargtnwsn gtnmgnytn gycaycartg ggcnytngr 660  
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acnytnmgnt gyccnytnaa rytngargcn gcnytnntgy armgncaayga ytggcayacn 960  
ytntgyaarg ayytnccnaa ygcnacngcn mgngarwsng aygngtggt ygtnytngr 1020  
aargtngayy tncayccna rytntgytty aargtnarc cntggtyws nttyggnaay 1080  
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 gayccnmng cngcncnytn nytnngcnytn ytncaygng cncnmgnc nytnytnytn 1740  
 ytnngentayt tywsnmgnytn ntgygcnaar ggngayathc cncncncnytn nmngcnytn 1800  
 ccmngntaym gnytnytnmg ngayytnccn mgnytnytnm gngcnytna ygcnmgnccn 1860  
 ttygcngarg cnacnwsntg gggngmnytn ggngcnmgnc armngmgnca rwsnmgnytn 1920  
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 <212> DNA  
 <213> Unknown

<220>  
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 Mus musculus

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 <222> (78)..(806)

<220>  
 <221> mat\_peptide  
 <222> (147)..(806)

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 Met Gly Ser Pro Arg Leu Ala Ala Leu Leu Leu  
 -20 -15  
  
 tct ctc ccg cta ctg ctc atc ggc ctc gct gtg tct gct cgg gtt gcc 158  
 Ser Leu Pro Leu Leu Leu Ile Gly Leu Ala Val Ser Ala Arg Val Ala  
 -10 -5 -1 1  
  
 tgc ccc tgc ctg cgg agt tgg acc agc cac tgt ctc ctg gcc tac cgt 206  
 Cys Pro Cys Leu Arg Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg  
 5 10 15 20  
  
 gtg gat aaa cgt ttt gct ggc ctt cag tgg ggc tgg ttc cct ctc ttg 254  
 Val Asp Lys Arg Phe Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu  
 25 30 35  
  
 gtg agg aaa tct aaa agt cct cct aaa ttt gaa gac tat tgg agg cac 302

Val	Arg	Lys	Ser	Lys	Ser	Pro	Pro	Lys	Phe	Glu	Asp	Tyr	Trp	Arg	His		
			40					45					50				
agg	aca	cca	gca	tcc	ttc	cag	agg	aag	ctg	cta	ggc	agc	cct	tcc	ctg	350	
Arg	Thr	Pro	Ala	Ser	Phe	Gln	Arg	Lys	Leu	Leu	Gly	Ser	Pro	Ser	Leu		
		55					60					65					
tct	gag	gaa	agc	cat	cga	att	tcc	atc	ccc	tcc	tca	gcc	atc	tcc	cac	398	
Ser	Glu	Glu	Ser	His	Arg	Ile	Ser	Ile	Pro	Ser	Ser	Ala	Ile	Ser	His		
	70					75					80						
aga	ggc	caa	cgc	acc	aaa	agg	gcc	cag	cct	tca	gct	gca	gaa	gga	aga	446	
Arg	Gly	Gln	Arg	Thr	Lys	Arg	Ala	Gln	Pro	Ser	Ala	Ala	Glu	Gly	Arg		
	85				90				95						100		
gaa	cat	ctc	cct	gaa	gca	ggg	tca	caa	aag	tgt	gga	gga	cct	gaa	ttc	494	
Glu	His	Leu	Pro	Glu	Ala	Gly	Ser	Gln	Lys	Cys	Gly	Gly	Pro	Glu	Phe		
				105				110					115				
tcc	ttt	gat	ttg	ctg	ccc	gag	gtg	cag	gct	gtt	cgg	gtg	act	att	cct	542	
Ser	Phe	Asp	Leu	Pro	Glu	Val	Gln	Ala	Val	Arg	Val	Thr	Ile	Pro			
			120				125						130				
gca	ggc	ccc	aag	gca	cgt	gtg	cgc	ctt	tgt	tat	cag	tgg	gca	ctg	gaa	590	
Ala	Gly	Pro	Lys	Ala	Arg	Val	Arg	Leu	Cys	Tyr	Gln	Trp	Ala	Leu	Glu		
		135				140						145					
tgt	gaa	gac	ttg	agt	agc	cct	ttt	gat	acc	cag	aaa	att	gtg	tct	gga	638	
Cys	Glu	Asp	Leu	Ser	Ser	Pro	Phe	Asp	Thr	Gln	Lys	Ile	Val	Ser	Gly		
	150					155					160						
ggg	cac	act	gta	gac	ctg	cct	tat	gaa	ttc	ctt	ctg	ccc	tgc	atg	tgc	686	
Gly	His	Thr	Val	Asp	Leu	Pro	Tyr	Glu	Phe	Leu	Leu	Pro	Cys	Met	Cys		
	165				170					175					180		
ata	gag	gcc	tcc	tac	ctg	caa	gag	gac	act	gtg	agg	cgc	aaa	agt	gtc	734	
Ile	Glu	Ala	Ser	Tyr	Leu	Gln	Glu	Asp	Thr	Val	Arg	Arg	Lys	Ser	Val		
				185					190					195			
cct	tcc	aga	gct	ggc	ctg	aag	ctt	atg	gct	cag	act	tct	ggc	agt	caa	782	
Pro	Ser	Arg	Ala	Gly	Leu	Lys	Leu	Met	Ala	Gln	Thr	Ser	Gly	Ser	Gln		
			200				205						210				
tac	gct	tca	ctg	act	aca	gcc	agc	ac								808	
Tyr	Ala	Ser	Leu	Thr	Thr	Ala	Ser										
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<213> Unknown																	
<400> 20																	
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			-20					-15					-10				
Leu	Ile	Gly	Leu	Ala	Val	Ser	Ala	Arg	Val	Ala	Cys	Pro	Cys	Leu	Arg		
		-5				-1	1				5						

Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg Val Asp Lys Arg Phe  
 10 15 20 25  
 Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu Val Arg Lys Ser Lys  
 30 35 40  
 Ser Pro Pro Lys Phe Glu Asp Tyr Trp Arg His Arg Thr Pro Ala Ser  
 45 50 55  
 Phe Gln Arg Lys Leu Leu Gly Ser Pro Ser Leu Ser Glu Glu Ser His  
 60 65 70  
 Arg Ile Ser Ile Pro Ser Ser Ala Ile Ser His Arg Gly Gln Arg Thr  
 75 80 85  
 Lys Arg Ala Gln Pro Ser Ala Ala Glu Gly Arg Glu His Leu Pro Glu  
 90 95 100 105  
 Ala Gly Ser Gln Lys Cys Gly Gly Pro Glu Phe Ser Phe Asp Leu Leu  
 110 115 120  
 Pro Glu Val Gln Ala Val Arg Val Thr Ile Pro Ala Gly Pro Lys Ala  
 125 130 135  
 Arg Val Arg Leu Cys Tyr Gln Trp Ala Leu Glu Cys Glu Asp Leu Ser  
 140 145 150  
 Ser Pro Phe Asp Thr Gln Lys Ile Val Ser Gly Gly His Thr Val Asp  
 155 160 165  
 Leu Pro Tyr Glu Phe Leu Leu Pro Cys Met Cys Ile Glu Ala Ser Tyr  
 170 175 180 185  
 Leu Gln Glu Asp Thr Val Arg Arg Lys Ser Val Pro Ser Arg Ala Gly  
 190 195 200  
 Leu Lys Leu Met Ala Gln Thr Ser Gly Ser Gln Tyr Ala Ser Leu Thr  
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 Thr Ala Ser  
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<210> 21

<211> 729

<212> DNA

<213> reverse translation

<220>

<221> misc\_feature

<222> (1)..(729)

<223> n may be a, c, g, or t

<400> 21

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gcngtnwsng cnmgngtngc ntgyccntgy ytnmgnwsnt ggacnwsnca ytggytnytn 120

gcntaymgng tngayaarmg nttygcnggn ytncartggg gntgggtycc nytnytnytn 180

mgnaarwsna arwsnccncc naarttygar gaytaytggm gncaymgnac nccngcnwsn 240  
 ttycarmgna arytnytngg nwsnccnwsn ytnwsngarg arwsncaymg nathwsnath 300  
 ccnwsnwsng cnathwsnca ymgnggncar mgnacnaarm gngcncarcc nwsngcngcn 360  
 garggmngng arcayytncc ngargcnggn wncaraart gyggnggncc ngarttywsn 420  
 ttygayytny tncngargt ncargcngtn mgngtnacna thccngcngg nccnaargcn 480  
 mgngtnmgny tntgytayca rtgggcnytn gartgygarg ayytnwsnws nccnttygay 540  
 acncaraara thgtnwsngg nggncayacn gtngayytn cntaygartt yytnytnccn 600  
 tgyatgtgya thgargcnws ntayytn car gargayacng tnmgnmgnaa rwsngtnccn 660  
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 acngcnwsn 729

<210> 22

<211> 2377

<212> DNA

<213> Unknown

<220>

<223> Description of Unknown Organism: primate; surmised  
Homo sapiens

<220>

<221> CDS

<222> (180)..(1874)

<400> 22

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 cagagcctgt tcttctactt acctgggccc ggagaagggtg gagggagacg agaagccgcc 120  
 gagagccgac taccctccgg gccagctctg tctgtccgtg gtggatctaa gaaactaga 179  
 atg aac cga agc att cct gtg gag gtt gat gaa tca gaa cca tac cca 227  
 Met Asn Arg Ser Ile Pro Val Glu Val Asp Glu Ser Glu Pro Tyr Pro  
 1 5 10 15  
 agt cag ttg ctg aaa cca atc cca gaa tat tcc ccg gaa gag gaa tca 275  
 Ser Gln Leu Lys Pro Ile Pro Glu Tyr Ser Pro Glu Glu Glu Ser  
 20 25 30  
 gaa cca cct gct cca aat ata agg aac atg gca ccc aac agc ttg tct 323  
 Glu Pro Pro Ala Pro Asn Ile Arg Asn Met Ala Pro Asn Ser Leu Ser  
 35 40 45  
 gca ccc aca atg ctt cac aat tcc tcc gga gac ttt tct caa gct cac 371  
 Ala Pro Thr Met Leu His Asn Ser Ser Gly Asp Phe Ser Gln Ala His  
 50 55 60  
 tca acc ctg aaa ctt gca aat cac cag cgg cct gta tcc cgg cag gtc 419  
 Ser Thr Leu Lys Leu Ala Asn His Gln Arg Pro Val Ser Arg Gln Val  
 65 70 75 80

acc tgc ctg cgc act caa gtt ctg gag gac agt gaa gac agt ttc tgc	467
Thr Cys Leu Arg Thr Gln Val Leu Glu Asp Ser Glu Asp Ser Phe Cys	
85 90 95	
agg aga cac cca ggc ctg ggc aaa gct ttc cct tct ggg tgc tct gca	515
Arg Arg His Pro Gly Leu Gly Lys Ala Phe Pro Ser Gly Cys Ser Ala	
100 105 110	
gtc agc gag cct gcg tct gag tct gtg gtt gga gcc ctc cct gca gag	563
Val Ser Glu Pro Ala Ser Glu Ser Val Val Gly Ala Leu Pro Ala Glu	
115 120 125	
cat cag ttt tca ttt atg gaa aaa cgt aat caa tgg ctg gta tct cag	611
His Gln Phe Ser Phe Met Glu Lys Arg Asn Gln Trp Leu Val Ser Gln	
130 135 140	
ctt tca gcg gct tct cct gac act ggc cat gac tca gac aaa tca gac	659
Leu Ser Ala Ala Ser Pro Asp Thr Gly His Asp Ser Asp Lys Ser Asp	
145 150 155 160	
caa agt tta cct aat gcc tca gca gac tcc ttg ggc ggt agc cag gag	707
Gln Ser Leu Pro Asn Ala Ser Ala Asp Ser Leu Gly Gly Ser Gln Glu	
165 170 175	
atg gtg caa cgg ccc cag cct cac agg aac cga gca ggc ctg gat ctg	755
Met Val Gln Arg Pro Gln Pro His Arg Asn Arg Ala Gly Leu Asp Leu	
180 185 190	
cca acc ata gac acg gga tat gat tcc cag ccc cag gat gtc ctg ggc	803
Pro Thr Ile Asp Thr Gly Tyr Asp Ser Gln Pro Gln Asp Val Leu Gly	
195 200 205	
atc agg cag ctg gaa agg ccc ctg ccc ctc acc tcc gtg tgt tac ccc	851
Ile Arg Gln Leu Glu Arg Pro Leu Pro Leu Thr Ser Val Cys Tyr Pro	
210 215 220	
cag gac ctc ccc aga cct ctc agg tcc agg gag ttc cct cag ttt gaa	899
Gln Asp Leu Pro Arg Pro Leu Arg Ser Arg Glu Phe Pro Gln Phe Glu	
225 230 235 240	
cct cag agg tat cca gca tgt gca cag atg ctg cct ccc aat ctt tcc	947
Pro Gln Arg Tyr Pro Ala Cys Ala Gln Met Leu Pro Pro Asn Leu Ser	
245 250 255	
cca cat gct cca tgg aac tat cat tac cat tgt cct gga agt ccc gat	995
Pro His Ala Pro Trp Asn Tyr His Tyr His Cys Pro Gly Ser Pro Asp	
260 265 270	
cac cag gtg cca tat ggc cat gac tac cct cga gca gcc tac cag caa	1043
His Gln Val Pro Tyr Gly His Asp Tyr Pro Arg Ala Ala Tyr Gln Gln	
275 280 285	
gtg atc cag ccg gct ctg cct ggg cag ccc ctg cct gga gcc agt gtg	1091
Val Ile Gln Pro Ala Leu Pro Gly Gln Pro Leu Pro Gly Ala Ser Val	
290 295 300	
aga ggc ctg cac cct gtg cag aag gtt atc ctg aat tat ccc agc ccc	1139
Arg Gly Leu His Pro Val Gln Lys Val Ile Leu Asn Tyr Pro Ser Pro	
305 310 315 320	

tgg gac caa gaa gag agg ccc gca cag aga gac tgc tcc ttt ccg ggg	1187
Trp Asp Gln Glu Arg Pro Ala Gln Arg Asp Cys Ser Phe Pro Gly	
325 330 335	
ctt cca agg cac cag gac cag cca cat cac cag cca cct aat aga gct	1235
Leu Pro Arg His Gln Asp Gln Pro His His Gln Pro Pro Asn Arg Ala	
340 345 350	
ggg gct cct ggg gag tcc ttg gag tgc cct gca gag ctg aga cca cag	1283
Gly Ala Pro Gly Glu Ser Leu Glu Cys Pro Ala Glu Leu Arg Pro Gln	
355 360 365	
gtt ccc cag cct ccg tcc cca gct gct gtg cct aga ccc cct agc aac	1331
Val Pro Gln Pro Pro Ser Pro Ala Ala Val Pro Arg Pro Pro Ser Asn	
370 375 380	
cct cca gcc aga gga act cta aaa aca agc aat ttg cca gaa gaa ttg	1379
Pro Pro Ala Arg Gly Thr Leu Lys Thr Ser Asn Leu Pro Glu Glu Leu	
385 390 395 400	
cgg aaa gtc ttt atc act tat tcg atg gac aca gct atg gag gtg gtg	1427
Arg Lys Val Phe Ile Thr Tyr Ser Met Asp Thr Ala Met Glu Val Val	
405 410 415	
aaa ttc gtg aac ttt ttg ttg gta aat ggc ttc caa act gca att gac	1475
Lys Phe Val Asn Phe Leu Leu Val Asn Gly Phe Gln Thr Ala Ile Asp	
420 425 430	
ata ttt gag gat aga atc cga ggc att gat atc att aaa tgg atg gag	1523
Ile Phe Glu Asp Arg Ile Arg Gly Ile Asp Ile Ile Lys Trp Met Glu	
435 440 445	
cgc tac ctt agg gat aag acc gtg atg ata atc gta gca atc agc ccc	1571
Arg Tyr Leu Arg Asp Lys Thr Val Met Ile Ile Val Ala Ile Ser Pro	
450 455 460	
aaa tac aaa cag gac gtg gaa ggc gct gag tcg cag ctg gac gag gat	1619
Lys Tyr Lys Gln Asp Val Glu Gly Ala Glu Ser Gln Leu Asp Glu Asp	
465 470 475 480	
gag cat ggc tta cat act aag tac att cat cga atg atg cag att gag	1667
Glu His Gly Leu His Thr Lys Tyr Ile His Arg Met Met Gln Ile Glu	
485 490 495	
ttc ata aaa caa gga agc atg aat ttc aga ttc atc cct gtg ctc ttc	1715
Phe Ile Lys Gln Gly Ser Met Asn Phe Arg Phe Ile Pro Val Leu Phe	
500 505 510	
cca aat gct aag aag gag cat gtg ccc acc tgg ctt cag aac act cat	1763
Pro Asn Ala Lys Lys Glu His Val Pro Thr Trp Leu Gln Asn Thr His	
515 520 525	
gtc tac agc tgg ccc aag aat aaa aaa aac atc ctg ctg cgg ctg ctg	1811
Val Tyr Ser Trp Pro Lys Asn Lys Lys Asn Ile Leu Leu Arg Leu Leu	
530 535 540	
aga gag gaa gag tat gtg gct cct cca cgg ggg cct ctg ccc acc ctt	1859
Arg Glu Glu Glu Tyr Val Ala Pro Pro Arg Gly Pro Leu Pro Thr Leu	
545 550 555 560	

cag gtg gtt ccc ttg tgacaccgtt catccccaga tcaactgaggc caggccatgt 1914  
 Gln Val Val Pro Leu  
 565

ttggggcctt gttctgacag cattctggct gaggctggtc ggtagcactc ctggctggtt 1974  
 tttttctgtt cctccccgag aggccctctg gccccagga aacctgttgt gcagagctct 2034  
 tccccggaga cctccacaca ccctggcttt gaagtggagt ctgtgactgc tctgcattct 2094  
 ctgcttttaa aaaaaccatt gcaggtgcca gtgtcccata tgttcctcct gacagtttga 2154  
 tgtgtccatt ctgggcctct cagtgccttag caagtagata atgtaaggga tgtggcagca 2214  
 aatggaaatg actacaaaca ctctcctatc aatcaattca ggctactttt atgagtttagc 2274  
 cagatgcttg tgtatcctca gaccaaactg attcatgtac aaataataaa atgtttactc 2334  
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 <212> PRT  
 <213> Unknown

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 Glu Pro Pro Ala Pro Asn Ile Arg Asn Met Ala Pro Asn Ser Leu Ser  
 35 40 45  
 Ala Pro Thr Met Leu His Asn Ser Ser Gly Asp Phe Ser Gln Ala His  
 50 55 60  
 Ser Thr Leu Lys Leu Ala Asn His Gln Arg Pro Val Ser Arg Gln Val  
 65 70 75 80  
 Thr Cys Leu Arg Thr Gln Val Leu Glu Asp Ser Glu Asp Ser Phe Cys  
 85 90 95  
 Arg Arg His Pro Gly Leu Gly Lys Ala Phe Pro Ser Gly Cys Ser Ala  
 100 105 110  
 Val Ser Glu Pro Ala Ser Glu Ser Val Val Gly Ala Leu Pro Ala Glu  
 115 120 125  
 His Gln Phe Ser Phe Met Glu Lys Arg Asn Gln Trp Leu Val Ser Gln  
 130 135 140  
 Leu Ser Ala Ala Ser Pro Asp Thr Gly His Asp Ser Asp Lys Ser Asp  
 145 150 155 160  
 Gln Ser Leu Pro Asn Ala Ser Ala Asp Ser Leu Gly Gly Ser Gln Glu  
 165 170 175

Met Val Gln Arg Pro Gln Pro His Arg Asn Arg Ala Gly Leu Asp Leu  
 180 185 190  
 Pro Thr Ile Asp Thr Gly Tyr Asp Ser Gln Pro Gln Asp Val Leu Gly  
 195 200 205  
 Ile Arg Gln Leu Glu Arg Pro Leu Pro Leu Thr Ser Val Cys Tyr Pro  
 210 215 220  
 Gln Asp Leu Pro Arg Pro Leu Arg Ser Arg Glu Phe Pro Gln Phe Glu  
 225 230 235 240  
 Pro Gln Arg Tyr Pro Ala Cys Ala Gln Met Leu Pro Pro Asn Leu Ser  
 245 250 255  
 Pro His Ala Pro Trp Asn Tyr His Tyr His Cys Pro Gly Ser Pro Asp  
 260 265 270  
 His Gln Val Pro Tyr Gly His Asp Tyr Pro Arg Ala Ala Tyr Gln Gln  
 275 280 285  
 Val Ile Gln Pro Ala Leu Pro Gly Gln Pro Leu Pro Gly Ala Ser Val  
 290 295 300  
 Arg Gly Leu His Pro Val Gln Lys Val Ile Leu Asn Tyr Pro Ser Pro  
 305 310 315 320  
 Trp Asp Gln Glu Glu Arg Pro Ala Gln Arg Asp Cys Ser Phe Pro Gly  
 325 330 335  
 Leu Pro Arg His Gln Asp Gln Pro His His Gln Pro Pro Asn Arg Ala  
 340 345 350  
 Gly Ala Pro Gly Glu Ser Leu Glu Cys Pro Ala Glu Leu Arg Pro Gln  
 355 360 365  
 Val Pro Gln Pro Pro Ser Pro Ala Ala Val Pro Arg Pro Pro Ser Asn  
 370 375 380  
 Pro Pro Ala Arg Gly Thr Leu Lys Thr Ser Asn Leu Pro Glu Glu Leu  
 385 390 395 400  
 Arg Lys Val Phe Ile Thr Tyr Ser Met Asp Thr Ala Met Glu Val Val  
 405 410 415  
 Lys Phe Val Asn Phe Leu Leu Val Asn Gly Phe Gln Thr Ala Ile Asp  
 420 425 430  
 Ile Phe Glu Asp Arg Ile Arg Gly Ile Asp Ile Ile Lys Trp Met Glu  
 435 440 445  
 Arg Tyr Leu Arg Asp Lys Thr Val Met Ile Ile Val Ala Ile Ser Pro  
 450 455 460  
 Lys Tyr Lys Gln Asp Val Glu Gly Ala Glu Ser Gln Leu Asp Glu Asp  
 465 470 475 480  
 Glu His Gly Leu His Thr Lys Tyr Ile His Arg Met Met Gln Ile Glu  
 485 490 495



Phe Ile Lys Gln Gly Ser Met Asn Phe Arg Phe Ile Pro Val Leu Phe  
                   500                                  505                                  510  
 Pro Asn Ala Lys Lys Glu His Val Pro Thr Trp Leu Gln Asn Thr His  
                   515                                  520                                  525  
 Val Tyr Ser Trp Pro Lys Asn Lys Lys Asn Ile Leu Leu Arg Leu Leu  
                   530                                  535                                  540  
 Arg Glu Glu Glu Tyr Val Ala Pro Pro Arg Gly Pro Leu Pro Thr Leu  
                   545                                  550                                  555                                  560  
 Gln Val Val Pro Leu  
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<210> 24  
 <211> 1695  
 <212> DNA  
 <213> reverse translation

<220>  
 <221> misc\_feature  
 <222> (1)..(1695)  
 <223> n may be a, c, g, or t

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 aayatggcnc cnaaywsnyt nwsngcnccn acnatgytnc ayaaywsnws nggngaytty 180  
 wsnrcargcnc aywsnacnyt naarytngcn aaycaycarm gncncngtnws nmgnrcargtn 240  
 acntgyytnm gnacncargt nytngargay wsnrgargayw snattytgymg nmgnrcayccn 300  
 ggnytnngna argcnttycc nwsnggntgy wsnrcngtnw sngarccngc nwsngarwsn 360  
 gtngtnngng cnytnccngc ngarcaycar ttywsnttya tggaraarmg naaycartgg 420  
 ytngtnwsnc arytnwsngc ngenwsnccn gayacnggnc aygaywsnga yaarwsngay 480  
 carwsnytn cnaaygcnws ngcngaywsn ytngngngnw snrcargarat ggtncarmgn 540  
 ccncarccnc aymgnaaymg ngcnggnytn gayytnccna cnathgayac nggntaygay 600  
 wsnrcarccnc argaygtnyt nggnathmgn carytngarm gncnytncc nytnacnwsn 660  
 gtntgytayc cncargayyt nccnmgnccn ytnmgnwsnm gngarttycc ncarttygar 720  
 ccncarmgnt ayccngcntg ygncaratg ytnccnccna ayytnwsncc ncaygcncn 780  
 tggaaytayc aytaycaytg yccnggnwsn ccngaycayc argtnccnta yggncaygay 840  
 tayccnmngng cngcntayca rcargtnath carccngcny tncnggnca rccnytnccn 900  
 ggngcnwsng tnmnggnytn ncayccngtn caraargtna thytnaayta yccnwsnccn 960

tgggaycarg argarmgncc ngcncarmgn gaytgywsnt tyccnggny t nccnmgnca y 1020  
 cargaycarc cncaycayca rccnccnaay mgngcnggng cncnngnga rwsnytn gar 1080  
 tgyccngcng arytnmgnc nccargtnccn carccnccnw snccngcngc ngtnccnmgn 1140  
 ccnccnwsna ayccnccngc nmngngnacn ytnaaracnw snaayytnc ngargarytn 1200  
 mgnaargtnt tyathacnta ywsnatggay acngcnatgg argtngtnaa rttygtnaay 1260  
 ttyytntyng tnaayggntt ycaracngcn athgayatht tygargaymg nathmgnggn 1320  
 athgayatha thaartggat ggarmgntay ytnmgngaya aracngtnat gathathgtn 1380  
 gcnathwsnc cnaartayaa rcargaygtn garggngcng arwsncaryt ngaygargay 1440  
 garcayggny tncayacnaa rtayathcay mgnatgatgc arathgartt yathaarc ar 1500  
 ggnwsnatga ayttymgntt yathccngtn ytnttyccna aygcnaaraa rgarcaygtn 1560  
 ccnactgggy tncaraayac ncaygtntay wsntggccna araayaaraa raayathytn 1620  
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<210> 25

<211> 1323

<212> DNA

<213> Unknown

<220>

<223> Description of Unknown Organism: rodent; surmised  
Mus musculus

<220>

<221> CDS

<222> (1)..(1026)

<400> 25

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gaa ctt gag agg tat cca atg aac gcc cag ctg ctg ccg ccc cat cct	96
Glu Leu Glu Arg Tyr Pro Met Asn Ala Gln Leu Leu Pro Pro His Pro	
20 25 30	
tcc cca cag gcc cca tgg aac tgt cag tac tac tgc ccc gga ggg ccc	144
Ser Pro Gln Ala Pro Trp Asn Cys Gln Tyr Tyr Cys Pro Gly Gly Pro	
35 40 45	
tac cac cac cag gtg cca cac ggc cat ggc tac cct cca gca gca gcc	192
Tyr His His Gln Val Pro His Gly His Gly Tyr Pro Pro Ala Ala Ala	
50 55 60	
tac cag caa gta ctc cag cct gct ctg cct ggg cag gtc ctt cct ggg	240
Tyr Gln Gln Val Leu Gln Pro Ala Leu Pro Gly Gln Val Leu Pro Gly	
65 70 75 80	

gca agg gca aga ggc cca cgc cct gtg cag aag gtc atc ctg aat gac	288
Ala Arg Ala Arg Gly Pro Arg Pro Val Gln Lys Val Ile Leu Asn Asp	
85 90 95	
tcc agc ccc caa gac caa gaa gag aga cct gca cag aga gac ttc tct	336
Ser Ser Pro Gln Asp Gln Glu Glu Arg Pro Ala Gln Arg Asp Phe Ser	
100 105 110	
ttc ccg agg ctc ccg agg gac cag ctc tac cgc cca cca tct aat gga	384
Phe Pro Arg Leu Pro Arg Asp Gln Leu Tyr Arg Pro Pro Ser Asn Gly	
115 120 125	
gtg gaa gcc cct gag gag tcc ttg gac ctt cct gca gag ctg aga cca	432
Val Glu Ala Pro Glu Glu Ser Leu Asp Leu Pro Ala Glu Leu Arg Pro	
130 135 140	
cat ggt ccc cag gct cca tcc cta gct gcc gtg cct aga ccc cct agc	480
His Gly Pro Gln Ala Pro Ser Leu Ala Ala Val Pro Arg Pro Pro Ser	
145 150 155 160	
aac ccc tta gcc cga gga act cta aga acc agc aat ttg cca gaa gaa	528
Asn Pro Leu Ala Arg Gly Thr Leu Arg Thr Ser Asn Leu Pro Glu Glu	
165 170 175	
tta cgg aaa gtc ttt atc act tat tct atg gac aca gcc atg gag gtg	576
Leu Arg Lys Val Phe Ile Thr Tyr Ser Met Asp Thr Ala Met Glu Val	
180 185 190	
gtg aaa ttt gtg aac ttt ctg ttg gtg aac ggc ttc caa act gcg att	624
Val Lys Phe Val Asn Phe Leu Leu Val Asn Gly Phe Gln Thr Ala Ile	
195 200 205	
gac ata ttt gag gat aga atc cgg ggt att gat atc att aaa tgg atg	672
Asp Ile Phe Glu Asp Arg Ile Arg Gly Ile Asp Ile Ile Lys Trp Met	
210 215 220	
gag cgc tat ctt cga gat aag aca gtg atg ata atc gta gca atc agc	720
Glu Arg Tyr Leu Arg Asp Lys Thr Val Met Ile Ile Val Ala Ile Ser	
225 230 235 240	
ccc aaa tac aaa cag gat gtg gaa ggc gct gag tcg cag ctg gac gag	768
Pro Lys Tyr Lys Gln Asp Val Glu Gly Ala Glu Ser Gln Leu Asp Glu	
245 250 255	
gac gag cat ggc tta cat act aag tac att cat cgg atg atg cag att	816
Asp Glu His Gly Leu His Thr Lys Tyr Ile His Arg Met Met Gln Ile	
260 265 270	
gag ttc ata agt cag gga agc atg aac ttc aga ttc atc cct gtg ctc	864
Glu Phe Ile Ser Gln Gly Ser Met Asn Phe Arg Phe Ile Pro Val Leu	
275 280 285	
ttc cca aat gcc aag aag gag cat gtg ccg acc tgg ctt cag aac act	912
Phe Pro Asn Ala Lys Lys Glu His Val Pro Thr Trp Leu Gln Asn Thr	
290 295 300	
cat gtt tac agc tgg ccc aag aat aag aaa aac atc ctg ctg cgg ctg	960
His Val Tyr Ser Trp Pro Lys Asn Lys Lys Asn Ile Leu Leu Arg Leu	
305 310 315 320	

ctc agg gag gaa gag tat gtg gct cct ccc cga ggc cct ctg ccc acc 1008  
 Leu Arg Glu Glu Glu Tyr Val Ala Pro Pro Arg Gly Pro Leu Pro Thr  
                   325                                  330                                  335

ctt cag gtg gta ccc ttg tgacgatggc cactccagct cagtgccagc 1056  
 Leu Gln Val Val Pro Leu  
                   340

ctgtttctcac agcattcttc tagcggagct ggctgggtggc acccaggccc tggaacacct 1116

cttctacaga gtcctctgtc tcctgagtct gagttgtcct cgctgggctt ccagagcttc 1176

agtgcctgga tgctgcaggt gacagaaaca aacatctatg accacaaaaa ctctcatcac 1236

ttcagctact tttatgagtc ggtcagatgc tctgtgtcct tagaccagtc taaatcatgc 1296

tcaaataata aaatgattat tctttgt 1323

<210> 26

<211> 342

<212> PRT

<213> Unknown

<400> 26

Gln Asp Leu Pro Gly Pro Leu Arg Ser Arg Glu Leu Pro Pro Gln Phe  
   1                                  5                                  10                                  15

Glu Leu Glu Arg Tyr Pro Met Asn Ala Gln Leu Leu Pro Pro His Pro  
                   20                                  25                                  30

Ser Pro Gln Ala Pro Trp Asn Cys Gln Tyr Tyr Cys Pro Gly Gly Pro  
                   35                                  40                                  45

Tyr His His Gln Val Pro His Gly His Gly Tyr Pro Pro Ala Ala Ala  
   50                                  55                                  60

Tyr Gln Gln Val Leu Gln Pro Ala Leu Pro Gly Gln Val Leu Pro Gly  
   65                                  70                                  75                                  80

Ala Arg Ala Arg Gly Pro Arg Pro Val Gln Lys Val Ile Leu Asn Asp  
                   85                                  90                                  95

Ser Ser Pro Gln Asp Gln Glu Glu Arg Pro Ala Gln Arg Asp Phe Ser  
                   100                                  105                                  110

Phe Pro Arg Leu Pro Arg Asp Gln Leu Tyr Arg Pro Pro Ser Asn Gly  
                   115                                  120                                  125

Val Glu Ala Pro Glu Glu Ser Leu Asp Leu Pro Ala Glu Leu Arg Pro  
   130                                  135                                  140

His Gly Pro Gln Ala Pro Ser Leu Ala Ala Val Pro Arg Pro Pro Ser  
   145                                  150                                  155                                  160

Asn Pro Leu Ala Arg Gly Thr Leu Arg Thr Ser Asn Leu Pro Glu Glu  
                   165                                  170                                  175

Leu Arg Lys Val Phe Ile Thr Tyr Ser Met Asp Thr Ala Met Glu Val

180	185	190
Val Lys Phe Val Asn Phe Leu Leu Val Asn Gly Phe Gln Thr Ala Ile		
195	200	205
Asp Ile Phe Glu Asp Arg Ile Arg Gly Ile Asp Ile Ile Lys Trp Met		
210	215	220
Glu Arg Tyr Leu Arg Asp Lys Thr Val Met Ile Ile Val Ala Ile Ser		
225	230	235
Pro Lys Tyr Lys Gln Asp Val Glu Gly Ala Glu Ser Gln Leu Asp Glu		
	245	250
Asp Glu His Gly Leu His Thr Lys Tyr Ile His Arg Met Met Gln Ile		
	260	265
Glu Phe Ile Ser Gln Gly Ser Met Asn Phe Arg Phe Ile Pro Val Leu		
	275	280
Phe Pro Asn Ala Lys Lys Glu His Val Pro Thr Trp Leu Gln Asn Thr		
	290	295
His Val Tyr Ser Trp Pro Lys Asn Lys Lys Asn Ile Leu Leu Arg Leu		
305	310	315
Leu Arg Glu Glu Glu Tyr Val Ala Pro Pro Arg Gly Pro Leu Pro Thr		
	325	330
		335
Leu Gln Val Val Pro Leu		
	340	

<210> 27  
 <211> 1026  
 <212> DNA  
 <213> reverse translation

<220>  
 <221> misc\_feature  
 <222> (1)..(1026)  
 <223> n amy be a, c, g, or t

<400> 27  
 cargayytnc cnggnccnyt nmgnwsnmgn garytnccnc cncarttyga rytngarmgn 60  
 tayccnatga aygcncaryt nytnccncn cayccnwsnc ncargcncc ntggaaaytgy 120  
 cartaytayt gyccnggngg nccntaycay caycargtnc ncayggnga yggntayccn 180  
 ccngcngcng cntaycarca rgtnytncar ccngcnytn cnggncargt nytnccnggn 240  
 gcnmgngcnm gnggnccnmg nccngtn car aargtnathy tnaaygayws nwsnccncar 300  
 gaycargarg armgnccngc ncarmngay ttywsnttyc cnmgnytncc nmngaycar 360  
 ytntaymgnc cncnwsnaa yggngtngar gncncngarg arwsnytn ga yytnccngcn 420  
 garytnmgnc ncayggnc ncargcnccn wsnytn gng cngtnccnmg nccnccnwsn 480

aayccnytn cnmgnngnac nytnmgnacn wsnaayytnc cngargaryt nmgnaargtn 540  
ttyathacnt aywsnatgga yacngcnatg gargtngtna arttygtnaa yttyytnytn 600  
gtnaayggnt tycaracngc nathgayath ttygargaym gnathmgngg nathgayath 660  
athaartgga tggarmgnta yytnmgngay aaracngtna tgathathgt ngcnathwsn 720  
ccnaartaya arcargaygt ngarggngcn garwsncary tngaygarga ygarcayggm 780  
ytncaayacna artayathca ymgntatg carathgart tyathwsnca rggwnsnatg 840  
aayttymgnt tyathccngt nytnnttyccn aaygcnaara argarcaygt nccnacntgg 900  
ytncaraaya cncaygtnta ywsntggccn aaraayaara araayathyt nytnmgnytn 960  
ytnmgngarg argartaygt ngcnccnccn mgnggncny tncnacnyt ncargtngtn 1020  
ccnytn 1026

<210> 28

<211> 207

<212> PRT

<213> Unknown

<220>

<223> Description of Unknown Organism:primate; surmised  
Homo sapiens

<400> 28

Arg	Lys	Val	Trp	Ile	Ile	Tyr	Ser	Ala	Asp	His	Pro	Leu	Tyr	Val	Asp
1				5					10					15	

Val	Val	Leu	Lys	Phe	Ala	Gln	Phe	Leu	Leu	Thr	Ala	Cys	Gly	Thr	Glu
			20					25					30		

Val	Ala	Leu	Asp	Leu	Leu	Glu	Glu	Gln	Ala	Ile	Ser	Glu	Ala	Gly	Val
			35					40					45		

Met	Thr	Trp	Val	Gly	Arg	Gln	Lys	Gln	Glu	Met	Val	Glu	Ser	Asn	Ser
	50						55				60				

Lys	Ile	Ile	Val	Leu	Cys	Ser	Arg	Gly	Thr	Arg	Ala	Lys	Trp	Gln	Ala
65					70					75				80	

Leu	Leu	Gly	Arg	Gly	Ala	Pro	Val	Arg	Leu	Arg	Cys	Asp	His	Gly	Lys
				85					90					95	

Pro	Val	Gly	Asp	Leu	Phe	Thr	Ala	Ala	Met	Asn	Met	Ile	Leu	Pro	Asp
			100					105					110		

Phe	Lys	Arg	Pro	Ala	Cys	Phe	Gly	Thr	Tyr	Val	Val	Cys	Tyr	Phe	Ser
		115					120					125			

Glu	Val	Ser	Cys	Asp	Gly	Asp	Val	Pro	Asp	Leu	Phe	Gly	Ala	Ala	Pro
	130					135					140				

Arg	Tyr	Pro	Leu	Met	Asp	Arg	Phe	Glu	Glu	Val	Tyr	Phe	Arg	Ile	Gln
145					150					155					160

Asp Leu Glu Met Phe Gln Pro Gly Arg Met His Arg Val Gly Glu Leu  
                   165                  170                  175

Ser Gly Asp Asn Tyr Leu Arg Ser Pro Gly Gly Arg Gln Leu Arg Ala  
                   180                  185                  190

Ala Leu Asp Arg Phe Arg Asp Trp Gln Val Arg Cys Pro Asp Trp  
                   195                  200                  205

<210> 29

<211> 208

<212> PRT

<213> Unknown

<220>

<223> Description of Unknown Organism:rodent; surmised  
       Mus musculus

<400> 29

Arg Lys Val Trp Ile Val Tyr Ser Ala Asp His Pro Leu Tyr Val Glu  
   1                  5                  10                  15

Val Val Leu Lys Phe Ala Gln Phe Leu Ile Thr Ala Cys Gly Thr Glu  
                   20                  25                  30

Val Ala Leu Asp Leu Leu Glu Glu Gln Val Ile Ser Glu Val Gly Val  
                   35                  40                  45

Met Thr Trp Val Ser Arg Gln Lys Gln Glu Met Val Glu Ser Asn Ser  
                   50                  55                  60

Lys Ile Ile Ile Leu Cys Ser Arg Gly Thr Gln Ala Lys Trp Lys Ala  
   65                  70                  75                  80

Ile Leu Gly Trp Ala Glu Pro Ala Val Gln Leu Arg Cys Asp His Trp  
                   85                  90                  95

Lys Pro Ala Gly Asp Leu Phe Thr Ala Ala Met Asn Met Ile Leu Pro  
                   100                  105                  110

Asp Phe Lys Arg Pro Ala Cys Phe Gly Thr Tyr Val Val Cys Tyr Phe  
                   115                  120                  125

Ser Gly Ile Cys Ser Glu Arg Asp Val Pro Asp Leu Phe Asn Ile Thr  
                   130                  135                  140

Ser Arg Tyr Pro Leu Met Asp Arg Phe Glu Glu Val Tyr Phe Arg Ile  
   145                  150                  155                  160

Gln Asp Leu Glu Met Phe Glu Pro Gly Arg Met His His Val Arg Glu  
                   165                  170                  175

Leu Thr Gly Asp Asn Tyr Leu Gln Ser Pro Ser Gly Arg Gln Leu Lys  
                   180                  185                  190

Glu Ala Val Leu Arg Phe Gln Glu Trp Gln Thr Gln Cys Pro Asp Trp  
                   195                  200                  205

<210> 30  
 <211> 190  
 <212> PRT  
 <213> Unknown

<220>

<223> Description of Unknown Organism:worm; surmised  
 Caenorabditis elegans

<400> 30

Val	Lys	Val	Met	Ile	Val	Tyr	Ala	Asp	Asp	Asn	Asp	Leu	His	Thr	Asp
1				5					10					15	
Cys	Val	Lys	Lys	Leu	Val	Glu	Asn	Leu	Arg	Asn	Cys	Ala	Ser	Cys	Asp
			20					25					30		
Pro	Val	Phe	Asp	Leu	Glu	Lys	Leu	Ile	Thr	Ala	Glu	Ile	Val	Pro	Ser
		35					40					45			
Arg	Trp	Leu	Val	Asp	Gln	Ile	Ser	Ser	Leu	Lys	Lys	Phe	Ile	Ile	Val
	50					55					60				
Val	Ser	Asp	Cys	Ala	Glu	Lys	Ile	Leu	Asp	Thr	Glu	Ala	Ser	Glu	Thr
65					70					75				80	
His	Gln	Leu	Val	Gln	Ala	Arg	Pro	Phe	Ala	Asp	Leu	Phe	Gly	Pro	Ala
				85					90					95	
Met	Glu	Met	Ile	Ile	Arg	Asp	Ala	Thr	His	Asn	Phe	Pro	Glu	Ala	Arg
			100					105					110		
Lys	Lys	Tyr	Ala	Val	Val	Arg	Phe	Asn	Tyr	Ser	Pro	His	Val	Pro	Pro
		115					120					125			
Asn	Leu	Ala	Ile	Leu	Asn	Leu	Pro	Thr	Phe	Ile	Pro	Glu	Gln	Phe	Ala
130						135					140				
Gln	Leu	Thr	Ala	Phe	Leu	His	Asn	Val	Glu	His	Thr	Glu	Arg	Ala	Asn
145					150					155					160
Val	Thr	Gln	Asn	Ile	Ser	Glu	Ala	Gln	Ile	His	Glu	Trp	Asn	Leu	Cys
				165					170					175	
Ala	Ser	Arg	Met	Met	Ser	Phe	Phe	Val	Arg	Asn	Pro	Asn	Trp		
			180					185					190		

<210> 31  
 <211> 178  
 <212> PRT  
 <213> Unknown

<220>

<223> Description of Unknown Organism:worm; surmised  
 Caenorabditis elegans



&lt;400&gt; 31

Phe Lys Val Met Leu Val Cys Pro Glu Val Ser Gly Arg Asp Glu Asp  
 1 5 10 15

Phe Met Met Arg Ile Ala Asp Ala Leu Lys Lys Ser Asn Asn Lys Val  
 20 25 30

Val Cys Asp Arg Trp Phe Glu Asp Ser Lys Asn Ala Glu Glu Asn Met  
 35 40 45

Leu His Trp Val Tyr Glu Gln Thr Lys Ile Ala Glu Lys Ile Ile Val  
 50 55 60

Phe His Ser Ala Tyr Tyr His Pro Arg Cys Gly Ile Tyr Asp Val Ile  
 65 70 75 80

Asn Asn Phe Phe Pro Cys Thr Asp Pro Arg Leu Ala His Ile Ala Leu  
 85 90 95

Thr Pro Glu Ala Gln Arg Ser Val Pro Lys Glu Val Glu Tyr Val Leu  
 100 105 110

Pro Arg Asp Gln Lys Leu Leu Glu Asp Ala Phe Asp Ile Thr Ile Ala  
 115 120 125

Asp Pro Leu Val Ile Asp Ile Pro Ile Glu Asp Val Ala Ile Pro Glu  
 130 135 140

Asn Val Pro Ile His His Glu Ser Cys Asp Ser Ile Asp Ser Arg Asn  
 145 150 155 160

Asn Ser Lys Thr His Ser Thr Asp Ser Gly Val Ser Ser Leu Ser Ser  
 165 170 175

Asn Ser